STUDIES OF THE SYNTHESES OF PIPERAZINE AND PYRAZINE IN VAPOR PHASE

By

C. E. GOULDING, JR.

A DISSERTATION PRESENTED TO THE GRADUATE COUNCIL OF
THE UNIVERSITY OF FLORIDA
IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE
DEGREE OF DOCTOR OF PHILOSOPHY

UNIVERSITY OF FLORIDA
May, 1946

PREFACE

The journal abbreviations used in this dissertation are the official abbreviations as used in "Chemical Abstracts" and in Abstracts of the Journal of the Chemical Society. The manner of listing references is the customary one used for technical works in organic chemistry. The material contained in this work is presented in a manner similar to that used for the articles in "Chemical Reviews".

In conformity with present usage in research communications, all temperatures are of the centigrade scale, the centigrade symbol is therefore omitted.

The melting points are open capillary melting points, unless indicated "(closed)". All melting points have been corrected so the melting points are given without the customary indication "(corr.)". The boiling points are given as the corrected boiling points for atmospheric pressures unless accompanied by a symbol designating pressures other than atmospheric.

The thermometers used for obtaining the melting points and boiling points were calibrated against a set of thermometers standardized by the Bureau of Standards.

TABLE OF CONTENTS

INTRODUCTION

The studies of the synthesis of piperazine and pyrazine have been carried out as a continuation of previous studies by Kitchen (124) and Goulding (104).

The previous works have dealt almost entirely with batch processes which necessarily limited the quantity of material made and greatly increased potential costs of the finished product. Kitchen (124) and Goulding (104) showed that piperazine could be made in liquid phase by the dehydration of N-(B-hydroxyethyl)ethene diamine. Goulding (104) has also shown that pyrazine could be prepared by treating piperazine with nitrobenzene in liquid phase. Since these attempts were batch processes, the present work was instigated to find a continuous process using the same starting material, N-(B-hydroxyethyl)ethene diamine, to prepare piperazine and pyrazine.

In order to obtain a continuous process, it was thought that a catalytic vapor-phase reaction would be the ideal way to obtain piperazine and pyrazine simultaneously from N-(B-hydroxyethyl)ethene diamine. This was accomplished by designing and constructing apparatus that would allow controlled heating of the catalytic mass and allow rigid control of the flow of vapor over the catalytic mass.

A systematic outline of procedures was followed in working with eight different catalysts. The temperatures investigated were 200°, 300°, and 400° at 50 mm. pressure. For each temperature, three experiments were run, by holding all but one variable constant. This variable was usually space velocity. When a catalyst showed that it could be heated to 400° without decomposing the vapor at 50 mm. pressure, other variables were introduced. One catalyst showed promising results and several other pressures were investigated.

The mechanics of the present work is the simultaneous removal of water and hydrogen by passing N-(B-hydroxyethyl)ethene diamine vapor through a tube containing a hot catalyst. In this process, there was always obtained small quantities of one or more of the following products; piperazine, pyrazine, ethylene diamine, ethanol amine, ethanol, acetaldehyde, diathylamine and ethylamine. Some of the products; ethylene diamine, ethanol amine, acetaldehyde, diethylamine, seem to be products of molecular fission while others; piperazine and pyrazine appear to be due to molecular rearrangement.

N-(B-hydroxyethyl)ethene diamine was previously synthesized by Knorr and Brownsden (126). It is one of the simplest of the amine alcohols and is available in commercial quantities as a by-product in the manufacture of polyethylene polyamines. This material, which was used as the primary starting material in the present synthesis, was obtained from Carbide and Carbon Chemical Corporation.

The physical properties and characteristics of some derivatives of N-(B-hydroxyethyl)ethene diamine have been summarized (124) and are presented here because the physical properties are not generally known, in spite of the fact that it is a commercial product. The derivatives of N-(B-hydroxyethyl)ethene diamine are essential for its recovery and identification from the residues in the synthesis of piperazine and pyrazine.

Summary of Properties of Derivatives of N-(B-hydroxyethyl)ethene diamine

Picrate:	M.p. 224° (dec.)	(124)
Dihydrochloride:	M.p. 114.3° -115.2°	(124)
Chloroplatinate:	M.p. 249° (dec.)	(126)
Phenylthiourea:	M.p. 131° -132°	
Physical state:	Light yellow hydroscopic liquid of medium viscosity of mildly ammonical odor	(42)
Emperical formula:	$C_4H_{12}N_2O$	
Structural formula:	$HOCH_2-CH_2-NH-CH_2-CH_2-NH_2$	
Molecular weight:	104.15	
Boiling points:	238° -240° at 752 mm.	(42)
	123° at 10 mm.	(124)
	118.5° at 7 mm.	(124)

Boiling points:	115.3° at 6.2 mm.	
Density:	d^{20}_{20} 1.0280-1.0330	(42)
	d^{25}_{4} 1.0254	(124)
Refractive index:	n^{25}_{D} 1.4851	(124)
	n^{25}_{D} 1.4843	(104)
Molecular refraction:	Mr^{25}_{D} 29.127	(104)

A. SYNTHESIS OF PYRAZINE

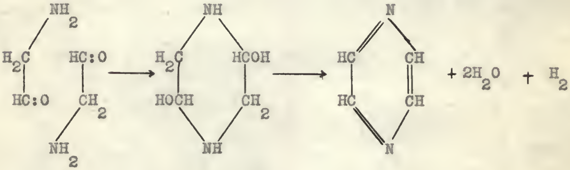
1. Review of Literature

There appears to be some question as to the discoverer of the pyrazine base. Gutknecht (107) discovered the tetramethyl pyrazine derivative but was unable to convert it into the true base. Several other derivatives of the base were investigated by Treadwell (218) and by Treadwell and Steiger (204). Similarly they were unable to obtain the pure base and Mason (139) was the first to suggest the name "Pyrazine" and to show the possible method of obtaining the true base. Mason insisted on this nomenclature in opposition to Victor Meyer (139) who advanced the name "Ketine".

Shortly after the discovery of tetramethyl pyrazine in 1879, several articles appeared in the literature describing the physical characteristics of pyrazine. Stoehr and co-workers (206, 207) and Wolff and co-workers (239) were the main contributors of this information.

Tanret (215) was probably the first to isolate the true base but due to its great affinity for carbon dioxide, the pyrazine base was isolated as the carbonate and was reported as ammonium carbonate. Tanret's experiments were repeated by Brandes and Stoehr (29) and the true base was isolated for the first time in 1896. Tanret, Brandes and Stoehr (29) found that pyrazine could be obtained by reacting glucose with ten parts of twenty-five per-cent ammonia for thirty-five hours at 100° and then distilling the base from a strong alkaline solution.

Wolff (237, 208) was the first to give a definite procedure for the preparation of the true base. This was accomplished by the slow distillation of pyrazine dicarboxylic acid. Wolff (238, 239), also, found that by heating amino acetaldehyde with oxalic acid that a twenty per-cent yield of pyrazine could be obtained.



Wolff found that amino acetaldehyde could be oxidized with bichloride of mercury to give a yield of twenty per-cent pyrazine but the base had to be steam distilled from the aqueous mixture and a large quantity of the solvent evaporated to obtain the pyrazine base. The base, pyrazine, was then removed from the concentrated solution by making the mercury salt of it, and then redistilling the pyrazine from a mixture of concentrated potassium carbonate and the mercury salt of the pyrazine base. This procedure is long, tedious, and expensive which renders it unprofitable for commercial purposes. The pure base was obtained as an oil which soon solidified to white needles.

Stoehr (205) prepared pyrazine by distilling piperazine, or its hydrochloride, with zinc dust. In this procedure, the yield was only about ten per-cent and the product obtained did not have the proper physical characteristics for pyrazine. He probably obtained a mixture of pyrazine, piperazine and some partially dehydrogenated piperazine. A large number of methyl substituted pyrazines and pyrazoic acids were also characterized in this work.

Stoehr (206, 207, 209) followed the probable procedure as predicted by Mason (139) and obtained pyrazine by first oxidizing the dimethyl pyrazine to the dicarboxylic derivative of pyrazine and then heating the acid in glacial acetic acid at 200°. From this he obtained a crystalline, colorless prism that melted at 47° and had a boiling point of 118 at 768.4 mm. pressure. Stoehr was the first to publish the true physical constants of the pyrazine base. The source of dimethyl pyrazine was obtained by heating a mixture of ammonicial salts with glycerol that was later added to acetaldehyde.

Bruhl (33) made a large number of observations on the refraction and dispersion of nitrogen compounds. The compounds examined in solutions of ethanol, ethylacetate, ethyl ether, and carbon disulfide. The molecular refraction, for the sodium line, and the dispersion, Mr - Ma, were calculated according to Lorenze's formula. Tutin (220) examined the obsorption spectra for many substituted pyrazine bases as well as for the salts of the pyrazoic acids. Schomaker and co-workers (190) investigated the electron diffraction of nitrogen compounds. He determined the interatomic distances and bond angles between the atoms. It was found in pyridine and pyrazine, that the C-N bond distance is greater than expected for Kekule resonance. By considering electron diffraction, electrical dipole moment, resonance energies, chemical activity and simple theoretical considerations, he concluded that pyrazine is more stable than pyridine. The work of Bruhl and Schomaker confirms the work and conclusions which were derived by Tutin.

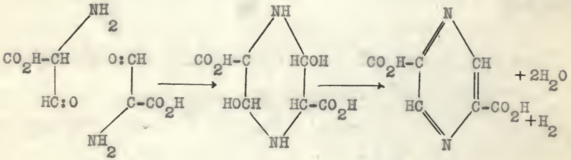
The relation between dipole moment and cohesion was studied by van Arkel (227). He studied 2, 5-dimethyl pyrazine and its picrate derivative. Van Arkel found that in unsaturated compounds the boiling point is effected in the same way by the kind and position of the substituent groups as in saturated compounds. However, in the transition of an alkyl group from an aliphatic union to an unsaturated one, the boiling point rises; the boiling point falls when a halogen atom goes through this transition.

Stoehr and Detert (211) investigated the possibilities of preparing pyrazine from tetra- and trimethyl derivatives of pyrazine. They found that when the tetra- and trimethyl derivatives were oxidized with potassium permanganate on a water bath, the tetra- and trimethyl derivatives were completely oxidized to the corresponding, rather unstable, tetra- or tricarboxylic derivative of pyrazine. When the tetra- and tricarboxylic derivatives of pyrazine were heated in water for two or three days, the acid lost carbon dioxide to form the dicarboxylic acid derivative of pyrazine.

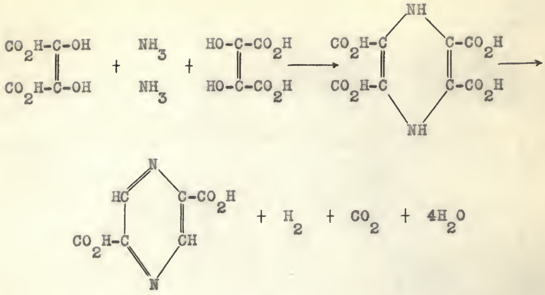
Fenton (87) reported that tetramethyl pyrazine could be obtained by condensing (B-bromo) or (B-hydroxy) laevulic acid with ammonia. When this compound was oxidized with potassium permanganate, the rather unstable tetracarboxylic pyrazine was formed. This work confirms the findings of Stoehr (211). When the potassium salt of this acid was heated in water at 200° the dicarboxylic acid of pyrazine was formed along with pyrazine and other products. He reported that hydroxypyruvic acid, $CH_2(OH)C:OCO_2H$, or dihydroxyacrylic acid, $CH(OH):C(OH)CO_2H$, would condense with ammonia in a manner similar to that in which Wolff (234, 238, 239) represents the formation of pyrazine from amino acetaldehyde.

Neresheimer (160) obtained several patents on pyrazine derivatives and their uses. Campbell (39) found that pyrazine could be prepared from isoquinaline derivatives. Scholl (189) working with azines and quinonediazides of the anthraquinone series found that pyrazoic acids could be formed by oxidation of the pyrazino compounds.

Horstman (115) found that when the ammonium or the sodium salt of dihydroxy maleic acid is mixed with an excess of strong aqueous ammonia and the mixture allowed to stand for one half hour on the water bath, pyrazine-2,5-dicarboxylic acid is formed. This is the same acid that Wolff (237) and Fenton (87) found. There are several possible explanations for this reaction. Carbon dioxide was found to be generated in the reaction. This would lead us to believe that the dihydroxy maleic acid lost carbon dioxide and formed tartronic aldehyde, $CHO\text{-}CH(OH)\text{-}CO_2H$, hydroxypyruvic acid, $CH_2(OH)\text{-}CH\text{:}0\text{-}CO_2H$, or dihydroxyacrylic acid, $CH(OH)\text{:}C(OH)\text{-}CO_2H$; condensation of any of these acids with ammonia would evidently take place in a manner similar to that in which Wolff (237) represents the formation of pyrazine from amino acetaldehyde. From tartronic semialdehyde, for example, the changes may be;



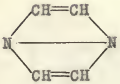
On the other hand, the initial product may be a tetracarboxylic acid which by oxidation and loss of carbon dioxide, gives the dicarboxylic acid as;



This type of reaction does not occur when the esters of dihydroxy maleic acid are treated with aqueous ammonia.

Goulding and Pollard (104) obtained pyrazine by treating piperazine with nitrobenzene. The unreacted piperazine and pyrazine were separated from the aniline and nitrobenzene by forming the piperazine and pyrazine carbonates. Pyrazine was obtained by the dry distillation of the mixed carbonates.

Wolff and Marburg (240) reported that by reacting semicarbazide with the hydrochloride of dihydroxymorpholine that morpholylcarbazone was formed from which pyrazine could be obtained when it was hydrolyzed with dilute hydrochloric acid at ordinary temperature. Carbamide was the main by-product. When dihydroxymorpholine was reacted with hydrazine or hydroxylamine, a product was formed that was extremely soluble in water and passed into pyrazine at zero degrees. From these reactions, he concluded that the two nitrogen atoms were linked together as;

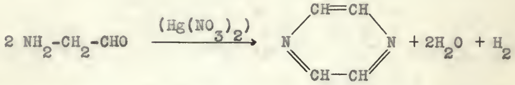


or

It was also reported, that diacetylhydrazine would yield pyrazine when treated with hydrochloric acid, but the mechanics of this reaction was not known. A yield of seventy-eight per-cent was claimed when diacetyl amine (CH_3-CO-NH-CO-CH_3) was treated with hydrochloric acid in the presence of hydroxylamine hydrochloride. All of these reactions seem to be carried out in a water solution, and there has been only one satisfactory method formulated for the removal of pyrazine from a water solution. This method is to form the mercuric chloride salt of pyrazine, and then distill the pyrazine away from the salt in an alkaline medium. This process would be highly unfeasible in the competition with some other method in which the high cost of reagents and manipulation would be the main considerations.

Neuberg and Kansky (159) reported that by reducing the hydrochloride of the esters of the amino acids with sodium amalgam, and then oxidizing with mercuric chloride, that pyrazine and pyrazine derivatives could be formed. In each reaction, Neuberg and Kansky isolated pyrazine or its methyl derivative as the mercuric chloride salt. The author has found this method to be very impractical for the isolation of pyrazine unless certain modifications are used instead of the conventional method of steam distilling. As shown later, certain modifications were resorted to in which there was less expense and mechanical loss. In the distillation of the pyrazine, from the mercuric chloride salt in strong alkali, recovery was poor due to oxidation and mechanical losses which became evident when the product had to be distilled twice before an anhydrous product was obtained.

Chichibobin and Shchukina (62) reported that, when monobromacetaldehyde was reacted with ammonia and then oxidized with a mercuric salt, that pyrazine could be obtained. The highest yield reported by them was seventeen per-cent. The pyrazine obtained was isolated as the mercuric salt.



The attempts to prepare pyrazine directly from the bromacetaldehyde and ammonia did not give satisfactory results, chiefly because of resin formation. When the bromine was replaced by ammonia, the yield was higher. This was accomplished by passing ammonia through the bromacetaldehyde-mercuric chloride mixture. Temperature, velocity of ammonia, and the choice of a solvent greatly influenced the resin formation.

A desmotropic form of diketopiperazine was found by Abderhalden and Schwab (9). When glycine, trysine and glycerol were mixed together and heated on an oil bath for five hours at 190°-200°, 3, 6-dihydroxy-1, 4-dihydropyrazine was obtained.

Brgstrom and Ogg (30) investigated the similarity between quinoxaline and pyrazine. In this investigation, the work of Gabriel and Sonn (90, 92) was confirmed. Brgstrom found that quinoxaline would add two molecules of sodium bisulfite. This bisulfite addition product decomposed on heating. From this, it was reasoned that pyrazine would act similarly. It was found, however, that pyrazine would not add sodium bisulfite or show any other chemical characteristics which are shown by quinoxaline. It was found that pyrazine would not react with hydrogen cyanide. Similarly, it was found that alkyl Grignards would not give N-substituted alkyl-pyrazines, and that pyrazine would not be attacked by iodine in liquid ammonia. The fact was established that pyrazine would be oxidized by iodine in alkaline solution.

Riesz (176) obtained a French patent for the use of pyrazine and substituted pyrazine as photographic emulsion desensitizers. Pyrazine compounds or its substituted derivatives were treated with substances capable of forming quaternary cyclic ammonium salts, and the products afterwards condensed with aromatic aldehydes are then reacted in aqueous solution with silver halide paper emulsions. The desensitized emulsion can be developed in relatively clear light without cloud formation. Gastaldi and Princivalle (101) confirmed and expanded the applications of Riesz (176).

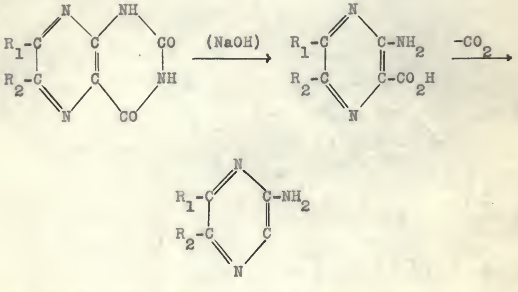
A German patent has recently been granted to Dorr and Mohring (78) in which the preparation of mixtures of volatile organic bases were obtained by heating sucrose or materials containing it with ammonia or its derivatives at 100° and a pressure of twenty to fifty atmospheres. The catalysts used were: a sulfite, an acid sulfite, animal charcoal or a metal salt, e.g., copper sulfate. The bases obtained were separated by distillion, after the addition of alkali.

Aston and co-workers (13) reported that pyrazine could be synthesized by the catalytic dehydrogenation and dehydration of ethanolamine. The most favorable conditions were found to be at a temperature of 300° with a copper catalyst. The catalyst was placed in a tube which acted also as a fractionating column. The fraction distilled in the range of 95°- 125° was taken as that which contained pyrazine. The pyrazine was isolated by acidifying the distillate with hydrochloric acid and then precipitating the pyrazine as the mercuric salt by adding an excess of a saturated solution of mercuric chloride. The pyrazine salt was recrystallized from dilute hydrochloric acid. The derivative was found to contain 56.86 per-cent mercury as compared with 57.05 per-cent for the calculated. This corresponds to the formula $(C_4H_4N_2)HgCl_2$. The yield of pyrazine obtained was 5.6 per-cent. Most of the amine disappeared by side reactions producing resins, which rendered the catalyst inactive. The pyrazine was recovered from the mercuric salt by distillation from concentrated alkali and then drying the distillate with solid potassium hydroxide and then redistilling. The fraction boiling at 112° - 114° at 730 mm. pressure was taken for the analysis. There was no information as to flow per gram of catalyst. This is the first attempt to prepare pyrazine by vapor-phase alkylation. The usefulness of the procedure, for the preparation of pyrazine, was not considered as satisfactory because of resin formation on the catalyst which rendered the latter inactive.

Spoerri and Erickson (201) investigated the Curtius and Hofmann degradation of pyrazine-2, 5-dicarboxylic acid. They found that the amide was stable toward both hypochlorous acids. It was found that the pyrazine nucleus would not nitrate but that the nucleus could be halogenated. The halogenated nucleus was found to be very unstable and decomposed at ordinary temperatures.

Hall and Spoerri (202) reinvestigated the work of Spoerri and Erickson (201) and found that 2-aminopyrazine could be prepared by treating pyrazine monocarboxylic amide with sodium hypochlorite. Two-aminopyrazine was found to have a melting point of 117° - 118°.

Ellingson (80, 81) found that sulfapyrazine could be prepared by treating the 2-aminopyrazine with p-amino-sulfonylchloride in a solvent of pyridine. The sodium salt was found to be the best preparation for oral use, having a pH of 9.3 in physiological saline solution. In later work, in conjunction with other workers (116, 117, 143, 217, 229), Ellingson found that 2-aminopyrazine carboxylic acid could be derived from lumazines which had previously been investigated by Kuhn and Cook (127a). Weijlard and co-workers (229), working with lumazine and substituted lumazines, found that 2-amino-3-carboxylic pyrazine could be readily decarboxylated to aminopyrazine.



The R_1 and R_2 can be hydrogen or any aryl or alkyl group.

This method of preparing 2-aminopyrazine seems to be a likely source of 2-aminoderivatives and since the yields are reported in the range of eighty per-cent it is much better to use this method of preparing 2-amino pyrazine than to attempt the amination of the pyrazine nucleus by the conventional use of sodium amide. Weijlard (229) found that, in contrast to lumazine, the substituted lumazines under the alkaline cleavage conditions did not form the hydroxy-acids and are stable to strong alkali at elevated temperatures. The substituted 2-amino pyrazoic acids are decarboxylated in eighty per-cent sulfuric acid. The alkaline cleavage of lumazine gives the 2-hydroxy-3-pyrazoic acid. This can be decarboxylated to give 2-hydroxypyrazine. It was found that when very dilute alkali or sulfuric acid cleavage of lumazine was carried out, that the 2-amino-3-pyrazoic acid could be prepared by this method.

Bilman (23) working with derivatives of pyrazine showed that N-benzylpyrazine carboxamide and N,N'-dibenzyl-2,3-dicarboxylic amido pyrazine possessed pronounced antispasmodic activity. Daniels (76) investigated the N,N'-pyrazine derivatives of sulfaminide. He demonstrated a method of preparing N- and N,N'-pyrazinoylsulfanilamides. In this work, he proposed the name of pyrazoic acid for pyrazine monocarboxylic acid.

Bills and co-workers (24) compared the uses of pyrazine carboxylic acid and pyrazine-2,3-dicarboxylic acid with nicotinic acid in curing glassitis and improving the well being of pellagrins. It was found that 500 to 800 milligrams of pyrazine carboxylic acid or pyrazine-2,3-dicarboxylic acid administered in divided doses five to eight times a day is effective in pellagrins, and safe for both pellagrins and normal human subjects. It was found that pyrazine carboxylic acid and pyrazine-2,3-dicarboxylic acid did not produce the vasodilator symptoms which often follow the use of large doses of nicotinic acid. Bean (20) working along the same trend, found that nicotinic acid and its sodium, ammonium, and ethanol amine salts and its ethyl ester produced vasodilation of the skin and an increase of temperature when given intravenously in twenty milligram doses. Pyrazine monocarboxylic acid produced only a slight rise in temperature, while all of the compounds were effective in treating pellagra. Bean confirmed the works of Bills and stated that pyrazine-2,3-dicarboxylic acid injections produced no vasodilation of the skin.

Three patents have been issued recently (73, 75, 149) to Merck and Company. These patents outline the preparation of and use of derivatives of pyrazine and substituted pyrazine and pyrazine acids.

Several investigators have investigated the antibiotic and pathological properties of pyrazine derivatives. Moller (153) investigated the use of mono- and dicarboxylic pyrazine in its action towards Proteus vulgaris and Streptococcus plantorum. It was found that these compounds have very marked control but little final effect on the organisms. McIlwain (151) attempted to show that a relationship existed between pyrazine derivatives and pyrazine di-N-oxides in antibiotics. The di-N-oxides inhibited the growth of Streptococcus hemolyticus and Cornynebacterium diptheriae.

Tamura (214) showed that sulfapyrazine in 2 x 10^{-4} mol. concentration induced complete bacteriostasis of Pasteurella tularensis with moderate and large inocula in a very favorable media. Endicott and Trevett (82, 219) investigated the use of sulfapyrazine in rats and mice. Trevett found that the lethal dose of sulfapyrazine in mice is approximately 0.6 grams per kilogram and that death occurred usually within twenty-four hours after injection. It was concluded that sulfapyrazine is as effective as sulfanilamide in the treatment of hemolytic streptococcual infections in mice. Schmidt (187) investigated the use of sulfapyrazine in mice infected with B-hemolytic streptococcus. It was concluded that single large doses were considerably more effective than similar doses of sulfathiozol, sulfapyridine and sulfanilimide and were essentially identical in activity with sulfadiazine. High blood levels persisted over long periods and were more easily produced than with most other sulfadrugs. Sesler (194) and Robinson (178) found that sulfapyrazine and sulfadiazine showed similar pathological changes in rats and mice. They also showed that sulfapyrazine gave higher blood levels and gave higher percentages of survivals than did sulfathiazol, sulfapyridine, sulfanilimide, when they were used in the treatment of pneumococcal, streptococcal and staphylococcal infections. Callomon (38) and Scudi (192) investigated the pathological effect on the kidneys of various sulfadrugs. It was found that sulfapyrazine produced no marked tissue damage in the kidneys.

The preparation of pyrazoic acids were investigated by Butlcher (37) and Gabriel (90, 92). Quinoxaline and its 2,3-dimethyl derivatives were oxidized to pyrazine-2,3-dicarboxylic acid and 5, 6-dimethylpyrazine-2, 3-dicarboxylic acid when heated with two per-cent potassium permanganate solution in the presence of potassium hydroxide. Butlcher investigated the methyl ester, metallic salts and the amides of the pyrazoic acids. Gabriel studied the decomposition products of pyrazoic acids and the preparation of aminopyrazine. Sausville (186) investigated the ionization constants of pyrazoic acids and the preparation of aminopyrazine derivatives. The formation of quinoxaline-2, 3-dicarboxylic acid was prepared by Chattaway and co-workers (43) by oxidation with permanganate solution, quinoxaline-2, 3-dicarboxy-o-phenylenediamine.

Gryszkiewrcz (106) and Hinkel (110) working with a polymer of hydrocyanic acid and Badshow (27) with an ethyl ester of cyanoacetic acid found that pyrazine-2, 3-dicyanopyrazine and pyrazine-2, 5, 6-tricarboxylic acid could be prepared.

Chandra De (79) carried out a series of experiments in which he demonstrated that dyes of various types could be prepared from pyrazine-2, 3-dicarboxylic acid. Ley and co-workers (137) investigated the use of pyrazine-2, 3-dicarboxylic acid as a quantitative colorimeteric reagent for iron.

The synthesis of pyrazine derivatives by the action of aromatic nitroso-o-hydroxy compounds on aldehydes in the presence of ammonia or primary aliphatic amines has been carried out by Lang (131). Lang was issued two patents which covered this synthesis (132, 133). Ochiai (163) and Calesue (65) working with catalytic reduction of isonitrosoacetylacetone and isonitrosoacetoethylacetate, respectively, found that 2,5-dimethyl-3, 6-diacetylpyrazine and 2, 4-dimethyl-3, 5-dicarbethoxypyrazine could be obtained. Gastaldi (93) reviewed the previous literature on isonitrosoketones and investigated the structure of the so-called bisulfite compounds of the isonitrosoketones. The behavior of isonitrosoketones toward potassium cyanide and their transformation into pyrazine derivatives. Aminoacetophenonesulfuric acids are reacted with potassium cyanide to give aminocyanoacetophenone sulfurous acid which when hydrolyzed with water condenses to form pyrazine derivatives: 2, 5-dicyanopyrazine, 2, 5-diphenyl-3-cyanopyrazine. Then these condensation products are heated with potassium hydroxide, hydroxypyrazines are obtained instead of the expected carboxylic acids. Sonn (200) prepared aminobenzylacetone hydrochloride by treating benzylisonitrosoacetone with stannous chloride in hydrochloric acid. When aminobenzylacetone hydrochloride is treated with aqueous sodium hydroxide a percipitate is formed which is converted into 2, 5-dimethyl-3, 6-dibenzylpyrazine with dilute sulfuric acid. Lang (131) found that hydroxydihydronaphthopyrazine could be prepared by dissolving alphanitrose-B-naphthol in aqueous sodium carbonate and adding ammonium chloride and acetic acid. Crippa (67) oxidized B-phenyl-1, 2-naphthaquinoxaline-3, 4-quinone with alkaline permanganate to obtain pyrazine-3-phenyl-5-carboxy-6-o-benzoic acid.

When (70) glutamic acid is acetylated in pyridine a ketone is formed from glutamic acid that is converted to to 2, 5-dimethylpyrazine-3, 6-dipropionic acid. In a simillar manner Fischer (89) made 2, 5-dimethyl-3, 6-diacetylpyrazine (86).

Sanna (184, 185) found that when indacyl halides, and substituted indacyl halides were heated with aqueous ammonia several products are formed, such as; diindalyldihydropyrazine and bis-(alpha-methylindacyl) pyrazine.

Bis-pentamethylenepyrazine was found to be formed when ammonia gas is reacted with chlorosuberone (103).

Godchot investigated this reaction and made many derivatives of bis-pentamethylenepyrazine. This compound was reduced in the presence of platinum by using sodium and anhydrous amyl alcohol. Three steroisomeric bis-pentamethylenepyrazine were formed by this method.

Avy (15) found that dichloro-tertiary alcohols reacted with ammonia, in absolute alcohol, to give 2, 2, 5, 5-tetramethyldihydropyrazine. Conant and Aston (66) found that 2, 2, 5, 5-tetramethyldihydropyrazine could be formed by oxidizing 2-methylpropanone with potassium ferricyanide. Piperazine is also formed in this reaction but the authors note that the ring reaction of nitrogen is obscure and unexplained.

The formation of a single diasterioisomer in the reaction of organomagnesium derivatives with aminoketones was found by Tiffeneau (216). By this method, Tiffeneau found that 2, 5-dimethyl-3, 6-diarylpyrazine could be synthesized.

In extending the reductions of the pyrimidine and pyrazine ring systems to dihydro derivatives by means of sodium thiosulfate, it was found that pyrimidine-MeI and the cetyl iodide analog, readily took up two atoms of hydrogen. By this method Karrer (121) produced 2, 5-dimethyl-N-methyl-6-hydropyrazine. Aston (11, 12) found that 2, 3, 5, 6-hexamethyl-N-methylpyrazine could be prepared. It was noted that the ring is broken upon standing in dilute alkali and that only one nitrogen is titrated with tenth normal acid.

Gastaldi (98, 99, 174) describes a method of preparing 2, 5- dimethyl-3, 6-dicyanopyrazine, 2, 5-dimethyl-6-hydropyrazine, and 2, 5-diphenyl-6-hydropyrazine. He shows how these compounds can be converted to the carboxylic acids and their esters.

The tetra- and pentamethylpyrazines were synthesized by Ochiai and co-workers (162) and by Wallach (228) and by De Paoline (167). Ochiai found that dioximes of o-diketones are not reduced to diamines but are first hydrolyzed to the mono-oxime which are then reduced to o-amino-ketones. Two moles of the enolic forms condensing with each other by loss of two molecules of water to form the dihydropyrazine which is easily oxidized to the pyrazine derivative in air.

The synthesis of 2, 3-dimethylpyrazine was found by Jorre (119) in 1907. Ethylene diamine was reacted with diacetyl in ether and the resulting 2, 3-dimethyl-5, 6-dihydropyrazine oxidized with Fehling's solution. Joiner (118) showed that methylpyrazines could be aminated with sodium amide in different solvents. Aston and co-workers (14) reacted methylpyrazine with sodium methylate and found that the pyrazine ring could be methylated in this manner.

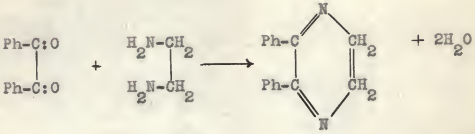
In the thermal decomposition of trans-1, 2-cyclobutane-bis-(trimethyl ammonium)hydroxide, Buchman (36) showed that tetraphenylpyrazine was formed. Meanwhile Takaki (212) reduced amarine with sodium amalgam and obtained tetraphenylpyrazine. Mason (143) working with monophenacylbenzylamine found that two molecules of the base would condense with the elimination of two molecules of water and 1, 4-dibenzyl-2, 5-diphenyldihydropyrazine is formed.

Abderhalden (2) and Karrer (120) found that O, O-dibenzyl-2, 5-dihydroxypyrazine could be formed when sarcosine anhydride reacted with benzylchloride. They found that this compound is decomposed by dilute sulfuric acid into aminoacetic acid and benzyl alcohol. Another method of preparing a tetraphenylpyrazine was found by Novelli (161) in which formamides are treated with anisoin at 180° to give tetra-p-methoxyphenylpyrazine. Pyrazine-2, 3-dibromo-6-methoxyphenyl was obtained from bromal and anisaldehyde cyanohydrin by Minovici (152).

Several diketopyrazine derivatives were investigated by Abenius (3, 4, 5). Rudenbury (180) reacted p-tolacylamine with aqueous ammonia in an atmosphere of carbon dioxide, and obtained dihydroditolylpyrazine. This compound is oxidized to ditolylpyrazine with a few drops of nitric acid or hydrogen peroxide or by boiling the alcoholic solution for a few minutes.

The preparation of 2, 3-diphenyl-5, 6-dihydropyrazine has been investigated extensively in the past forty years. The main interest in this compound was enhanced by the demand for aminopyrazine which can be derived from the 2, 3-dicarboxylic pyrazine. Amendsen (8), Hieber (108), Mason (139, 142) and van Alphen (223) synthesized 2, 3-diphenyl-

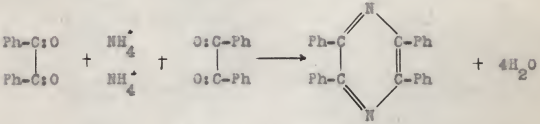
5, 6-dihydropyrazine from benzil and ethylene diamine.



This compound readily loses hydrogen by air oxidation or on heating in alcoholic solution.

When alpha-aminoketones are liberated from their salts, they undergo oxidation and condensation, yielding disubstituted pyrazines. Gabriel (93) found that alpha-bromoacetophenone is converted by aqueous ammonia into diphenyldihydropyrazine and traces of diphenylpyrazine. Tutin (221), in a similar manner, prepared 2, 5-diphenylpyrazine by treating chloroacetophenone with ammonia in the presence of aluminum chloride. Ochiai (164) and Petrow characterized 2, 5-diphenylpyrazine and its derivatives. Ochiai found that he could nitrate the pyrazine ring when it has two substituted phenyl groups present on the ring. Gabriel (96) confirmed some of the work of Tutin (221) and showed that 2, 6-diphenylpyrazine could be formed by the methods of Tutin. Gabriel (94) working with alpha-aminoacetophenone found that dihydroxyphenylpyrazine is formed by the action of ammoni on the hydrochloride salt of alpha-aminoacetophenone. This affirms the earlier work of Gabriel and disproves some of the work of Meyer (139).

Davidson (77) and Leslie (134) studied the action of liquid ammonia and solutions of ammonium salts on benzoin. Tetraphenylpyrazine was formed by similar methods.



In a similar method, Curtus (69) worked with hydrazine hydrate and otho-diketone. He found that this method would synthesize tetra-p-tolylpyrazines in a satisfactory manner.

Raiziss and Clemence (175) investigated the therapeutic activities of a number of different derivatives of pyrazine. Among these were the N-sulfanilimide derivatives of pyrazine.

The characteristics of pyrazine have been summarized by Mulliken (156) as: prisms from water, alcohol, and ether. The prisms of pyrazine are soluble in water, alcohol, and ether. Pyrazine is a weak base which fumes with hydrochloric acid.

In the recent work, carried out by Pfann (169), it was found that pyrazine formed an azeotrope with water. No azeotrope was found when pyrazine was distilled with methanol or ethanol. The refractive indices of the pyrazine-water solutions were found to be nearly linear functions of weight concentrations.

Kitchen (124) reported traces of pyrazine as a by-product in the synthesis of piperazine when Raney-Nickel was used as the catalyst for the ring closure of N-(B-hydroxyethyl)ethene diamine.

Summary of Properties of Pyrazine

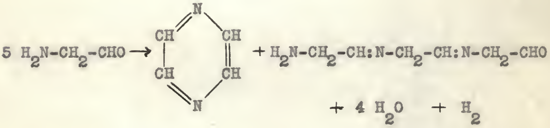
Physical state:	volatile, hygroscopic solid having weak basic characteristics.	
Melting point:	47°- 48°	(104)
Boiling point:	117°-118° at 758 mm.	
	115.8°-116.3° at 760.5 mm.	(104)
	112°-114° at 730 mm.	(13)
Picrate:	M. p. 156°-157°	(156)
Silver Nitrate:	M. p. 257°	(237)
Mercuric chloride:	M. p. 273°	(209)
Aurechloride:	M. p. 245°	(205)
Aurichloride:	M. p. 202°	(159)
Sulfate:	M. p. 136°-137°	(209)
Nitrate:	M. p. 150°	(104)
Density:	$d_4^{60.9}$ 1.031 g./cc.	(104)
Refractive index:	$n_D^{60.9}$ 1.4953	(104)

2. Discussion

There are many methods known for the synthesis of pyrazine but most of them are inpractical for commercial production. Of the few syntheses that give pyrazine there appears to be only one that can be feasible as a commercial process. Aston and co-workers (13) showed that this method would give pyrazine by the catalytic vapor-phase dehydrogenation and dehydration of ethanol amine. Most of the amine disappeared, in this reaction, to give rise to resin formation. It is assumed that this reaction could be made of commercial importance if a better catalyst were discovered whereby the side reactions could be either eliminated or limited to a small degree. With this idea in mind the present investigation was carried out. By the simultaneous dehydration and dehydrogenation of N-(B-hydroxyethyl)ethene diamine in catalytic vapor-phase, a continuous process for the production of pyrazine has been demonstrated.

There are only a few syntheses that give pyrazine as a final product, without going through a series of oxidations and decarboxylation. A synthesis of this type, in producing pyrazine, is not very satisfactory because the product is always obtained in a water solution. Wolff (208, 237) demona synthesis of this type by distilling pyrazoic acid slowly from an alkaline solution. As the pyrazoic acid was decarboxylated, the pyrazine steam distilled. To obtain the pyrazine from the distillate, it was necessary to form the mercuric chloride salt which was then distilled from saturated potassium hydroxide solution to recover the pyrazine. To remove the water associated with the distillate, it was necessary that the distillate be treated with solid potassium hydroxide to take up the water. The solidified mixture was then dry distilled to recover the anhydrous pyrazine.

In all of these reactions there appears to be the accepted idea that a condensation must occur between an aldehyde or ketone and an amine or ammonia, with the elimination of a molecule of water. A condensation of this type creates an unsaturated linkage that seems to make excess hydrogen atoms more liable than they would be if the unsaturated linkages were not present. An example of this type of condensation was demonstrated by Wolff (238, 239), in which amino acetaldehyde was condensed with itself, splitting out two molecules of water, to give pyrazine. In a synthesis of this type there is a possibility of linear side reactions which would make the cyclic condensation less feasible.



Another type of synthesis is demonstrated by Fenton (87), in which hydroxypyruvic acid is condensed with ammonia. This type of reaction always appears to produce a low yield because ammonia ia a poor alkylating agent. There is, at the same time, evidence of side reactions which would also account for poor yields in the desired product, pyrazine.

3. Catalytic Alkylation

The present investigation of catalytic vapor-phase alkylation was prompted by the results of other investigators. The vapor-phase alkylation of aromatic amines with alcohols has been investigated by Maihl and de Godon (144), Brown and Reid (32), and by Shuikin and co-workers (195, 197). They obtained high yields and found that effective catalysts were oxides of aluminum, titanium, iron and silica gel. The simultaneous dehydration of ethanol and ammonia using alumina catalyst have been reported by Shuikin and co-workers (196). Aston (13) reported the catalytic vapor-phase alkylation of ethanol amine with copper chromite catalyst.

B. SYNTHESIS OF PIPERAZINE

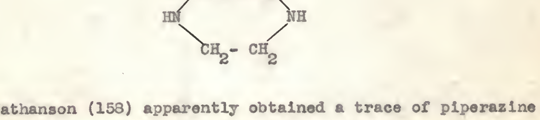
1. Review of the Literature

Piperazine, first prepared by Clooz in 1853 (68), has been the subject of a large volume of research in the ninety-three years that it has been known. Numerous uses have been developed for piperazine and piperazine derivatives. Use is made of piperazine as a reagent for preparing solid derivatives of fatty acids for identification purposes as shown by (170); the preparation of the piperazine salts is unique and their melting points are very sharp. Nine patents relating to piperazine and piperazine products have been granted within the past fifteen years, eight (60, 63, 64, 83, 84, 165, 177, 191) relate to medicinals; one (199) to a series of local anesthetics; one (31) to the use of piperazine as a corrosion inhibiter; and one (32) to a series of emulsifying and wetting agents. Biedebach and Weigand (22) suggests the use of piperazine in emulsions.

A potential use of piperazine which may soon utilize large quantities of piperazine per year is as a source of pyrazine ring for the synthesis of sulfapyrazine. The methods of pyrazine synthesis are unsatisfactory as a rule, and it is thought that catalytic dehydrogenation of piperazine may be successfully used as a source of pyrazine. Sulfapyrazine was synthesized in 1941 by Ellingson (80, 81); the recent preliminary report by Ruegsegger (181) upon the pharmacological action of sulfapyrazine indicates that this addition to the list of sulfadrugs will become of wide application in pneumonia treatment.

Since the initial synthesis of piperazine, numerous methods of manufactureing piperazine have been published. At the present time, there seems to be only one synthesis of piperazine that demonstrates economic feasibility (104, 124). Consequently piperazine has remained high in price, and at the present time it is not available on the market. There are, at the present time, eight patents (40, 41, 63, 64, 105, 128, 172, 232, 233), and a patent application (171) relating to three different processes for the commerical production of piperazine.

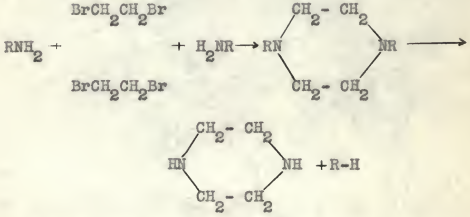
Piperazine was first obtained by Clooz (68) in investigating the reaction of alcoholic ammonia with ethene dichloride and ethene dibromide:



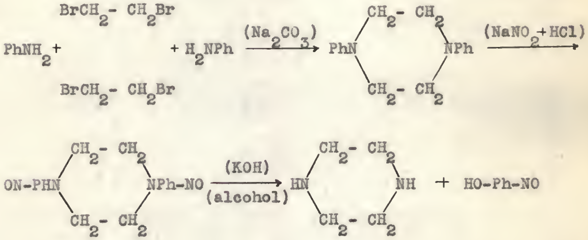
Nathanson (158) apparently obtained a trace of piperazine by the treatment of ethene dichloride with alcoholic ammonia.

The reaction also was investigated by Hofmann (113). This reaction, however, is of little value for the synthesis of piperazine, for piperazine is only a minor product; various polyamines, such as ethene diamine, diethene triamine, and triethene tetramine are formed in the same process (114). A similar method was used by Sieber (198) for the synthesis of piperazine in which he reacted ethene diamine and ethene dibromide. Sanna and Oliveria (182) recently have described an improved process which involves the use of very concentrated ammonia and ethene dibromide.

Processes were later developed for the synthesis of piperazine which gave somewhat better yields than those of the direct alkylation of ammonia. These processes involved the alkylation of a compound RNH_2 containing a primary amino group by means of ethene dihalide and subsequent removal of the R. group by various methods.



The most widely used process of this type was the one which was developed by Bischler in 1891 (26). Bischler applied the well known reaction, the alkali hydrolysis of nitroso-substituted arylamines, to the preparation of piperazine by splitting N, N'-bis-(p-nitrosophenyl)-piperazine with alcoholic potassium hydroxide.



The intermediate dinitroso compound had been previously prepared by Morely (155) through treatment of N, N'-diphenyl piperazine with sodium nitrite and dilute hydrochloric acid. Sodium carbonate was used to remove the HBr in the ring closure reaction between aniline and ethene dibromide.

Various German patents have been granted relating to this type of process. One of these (45) utilizes distillation with alcoholic potassium hydroxide or heating with an alkaline earth hydroxide in a closed vessel. Another method (57) carried out by boiling with dilute alkali as the method of hydrolysing the dinitroso compound. A third process (55) describes the preparation of piperazine by the gradual introduction of an alkaline solution of sodium nitrite and

N, N'-bis-(p-hydroxyphenyl)-piperazine into ten per-cent hydrochloric acid with cooling, which is then followed by hydrolysis.

A procedure was described by Morera (154), in which he claimed good results, by boiling aniline and ethene dibromide together for three hours; the base is liberated by soda and the liberated base extracted with benzene. The extract is distilled at atmospheric pressure to remove the benzene and then distilled in vacuum; the product is nitrosified with sodium nitrite-hydrochloric acid mixture in ice and is then hydrolyzed with sodium hydroxide.

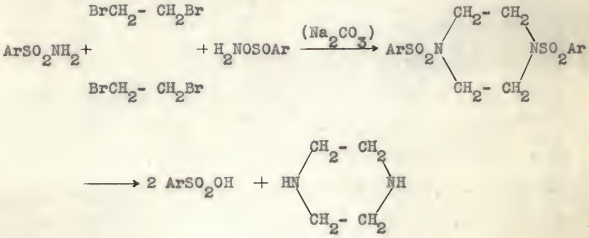
Sanna and Oliverio (185) describes a shortened process in which p-nitrosoaniline is utilized for the alkylation of ethene dibromide. The p-nitrosophenol obtained in the hydrolysis reaction can be recovered and converted to the p-nitrosoaniline.

According to a German patent (47) the hydrolysis of aromatic nitroso derivatives is generally facilitated by treatment with sodium bisulfite or some other form of sulfur dioxide. Sulfonic acid derivatives are formed which readily rearrange with loss of the amino group. A patent issued to Volkmann (19, 226) applies this method to the hydrolysis of N, N'-bis-(p-nitrosophenyl)-piperazine. Pratt and Young (173) gave details of an improved synthesis of piperazine from aniline and ethene dibromide which utilized the sodium bisulfite hydrolysis. A German patent (46) describes a process of obtaining piperazine by treating sulfonic acids of nitrosified diphenylpiperazine with alkali. Another patent issued to Marjet (48, 146) stated that a sulfonic acid, or preferably a polysulfonic acid, of a diaryl piperazine could be hydrolyzed by alkali to yield piperazine. Busherer (35) reports a small yield of piperazine was obtained by sulfonation of N, N'-bis-(naphthyl)piperazine and then treating the sulfonic acid with bisulfite in sodium hydroxide solution in a sealed tube at 140-160°.

Piperazine has been prepared by the hydrolysis of many aryl-substituted piperazines. Gabriel and Stelzner (91) prepared 1, 4-dibenzylpiperazine by treating bromoethyl benzyl amine with excess alkali. The 1, 4-dibenzylpiperazine was then hydrolyzed by using ten per-cent hydrochloric acid at 100° (56). The hydrolysis of many aryl-disubstituted piperazines has been carried out by Majert (145) in an alkaline medium and then steam distilling the piperazine into an acid solution. The piperazine was recovered as the hydrochloride salt which would yield the piperazine molecule when it was distilled in the presence of alkali. The hydrolysis of alpha and beta di-naphthylpiperazines may be carried out in acid solution or with solutions of calcium and zinc chlorides at 250°, (56).

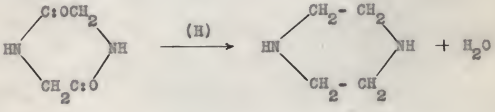
A German patent (52) states that the diaryl piperazines may be hydrolyzed by other means than by acids and alkali. This was carried out by suspending the piperazine compound in dilute sulfuric acid and then treating the suspension with sodium dichromate.

The alkylation of an aryl sulfonamide with ethene dihalide, followed by the hydrolysis of the diarylsulfonyl piperazine would serve as another process for the synthesis of piperazine. The process which consists of:

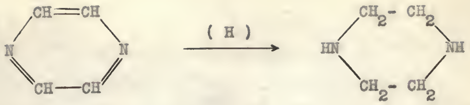


Markwald patented this process in 1893 (157). The hydrolysis can be carried out in several ways; by means of concentrated sulfuric acid in an open vessel (51), by autoclaving with dilute acid at 200-250°, and by the introduction of sodium into boiling amyl alcohol suspension of the compound, followed by steam distillation, (53). Chlorosulfonic acid was shown in a German patent to serve as a suitable hydrolyzing agent when poured into water, (59). Vinaver (222) found that the diarylpiperazine could be hydrolyzed by dilute sulfuric acid, in an open vessel at 180-200°. He also found that piperazine could be prepared by hydrolyzing di-p-toluenesulfonyl piperazine with sulfuric acid.

Several articles have appeared on the reduction of other six membered rings containing nitrogen in the 1- and 4- positions to piperazine. A German patent was granted on the reduction of 2, 5-diketopiperazine by means of zinc dust and aqueous alcoholic sodium hydroxide. A similar process was carried out in anhydrous amyl alcohol with sodium, (49). The reduction of 3, 6-diketopiperazine was also investigated by Abderhalden (1). The reagents tried by Abderhalden includes zinc in acetic acid, zinc in hydrochloric acid, Devarda's alloy plus dilute alkali, sodium and alcohol, and calcium and water in the presence of carbon dioxide. Abderhalden and co-workers found that electrolytic reduction was not as satisfactory as the chemical reduction. Karrer (120) reduced dihydroxy dihydropyrazine. Wrede (241) and co-workers, however, reported that electrylytic reduction is the best method for the reduction of cyclic lactim, glycine anhydride, to piperazine.



They obtained a yield of twenty-seven per-cent in this work (241). Wolff (236) reduced pyrazine, the unsaturated piperazine ring, to piperazine by means of sodium and alcohol.

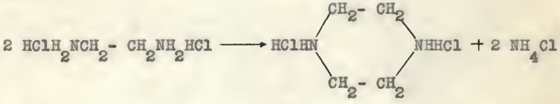


The methods of preparing piperazine by hydrolyzing some other products are most generally accompanied by low yields and the expense and labor is large in proportion to the quantity and value of the product obtained. Many direct alkylations have been attempted to eliminate the necessity of forming an intermediate compound which would require hydrolysis. In hydrolyzing an intermediate product, the process is confronted with many unfavorable aspects such as steam distillation, concentration of large volumes and mechanical losses. An early attempt to synthesize piperazine is described in a German patent (50), in which the synthesis is accomplished by the heating of a sodium glycollate with an acid derivative of ethene diamine at 250-300°. The basis of another process was the heating of a sodium compound of diacylethene diamine with anhydrous glycol or ethene dibromide in xylene as diluent at 200°, (54). This process is not considered of very great importance because of the equipment that is required to carry out the reaction.

A ninety per-cent yield of piperazine was claimed by Garelli and Racciu (97) by dehydrating ethanolamine with an excess of ninety per-cent sulfuric acid. This reaction was carried out at 90° - 140° for a short period of time. This same procedure was investigated by Rollins and Calderwood (179) and they were unable to obtain piperazine. They did obtain, however, aminoethane sulfonic acid.

Grosberg (105) obtained a patent for the synthesis of piperazine. The procedure consisted of heating ethene diamine with an ester such as ethene glycol monoacetate for twenty-four hours at 200°- 300°. Zinc chloride was suggested as a possible catalyst for this reaction.

The reactions which involve the alkylation of an amine with an amine with the elimination of ammonia have been applied to the preparation of piperazine. This reaction was the basis of the reaction carried out by Ladeburg (129) and Abel (130), in which they prepared piperazine by heating ethene diamine dihydrochloride.



The piperazine obtained here was the hydrochloride salt and is not recommended as an economical method for the preparation of anhydrous piperazine. Hofmann (112) carried the investigation further and found that the hydrochloride of piperazine is formed by heating the hydrochloride of diethene triamine or of triethene triamine. The by-product in this reaction as well as that of Ladenburg and Abel is ammonium chloride. Piperazine was also obtained by heating ethene diamine hydrochloride. Several patents have been granted to Wilson (40, 41, 231, 232, 233) and Carbide and Carbon Chemical Corporation on this process. The ring closure of diethene triamine and one of its hydrochlodires was effected by heating to 220° under a pressure. The piperazine was obtained by distillation from an alkaline medium.

Kyrides (128) perfected a process in the formation of piperazine by splitting ammonia from diethene triamine by a catalytic procedure. The reactants were heated to 200-300° for twenty-four hours in the of a catalyst. Nickel, platinum, cobalt and copper, etc., in the finely divided state were found to be suitable catalysts. Yields of fifty per-cent were claimed for this process but actual practices gave much lower yields.

Kitchen found that anhydrous piperazine could be synthesized by the catalytic dehydration of N-(B-hydroxyethyl) ethene diamine in a pressure bomb (124). A similar method was outlined in a patent application granted to Poppenberg (172). In this process the ring closure was effected by the removal of water at a temperature of 200-300° in the presence of ammonium salts. The product obtained, however, was in the form of a salt and is therefore a much more complicated process than that of Kitchen's. The ring closure of N-(B-hydroxyethyl)ethene diamine was shown by Kitchen to give piperazine in fifty per-cent yields in the presence of an inert solvent. The catalysts used consisted of copper-chromium oxide, Raney-Nickel, activated alumina, silica gel, Fuller's earth, barium oxide, chromic oxide, cupric oxide, reduced iron, palladium, stannous oxide, Norite and vermiculite. The highest yield of fifty per-cent was obtained with Raney-Nickel. In this process Kitchen claimed that there was a small yield of pyrazine formed. This work was repeated by Goulding (104) and it was found that there was an excess of hydrogen present in the reaction bomb and that no pyrazine could be found as stated by Kitchen.

The catalytic ring closure of N-(B-hydroxyethyl)ethene diamine, using Raney-Nickel, was investigated by Goulding (104) and it was found that a yield of seventy per-cent anhydrous piperazine could be obtained. This reaction was carried out in anhydrous butanol-1, using Raney-Nickel in the high pressure bomb at 200°.

Sanna (183) found that piperazine could be prepared by treating p-nitrosoaniline with ethene dibromide in the presence of potassium carbonate and hydrolyzing the bis-(p-nitrosophenyl)piperazine. He also found that the disubstituted piperazine could be hydrolyzed with ammonia and ammonium chloride instead of potassium hydroxide so that in addition to piperazine the p-nitrosoaniline is recovered in practically quantitative yields.

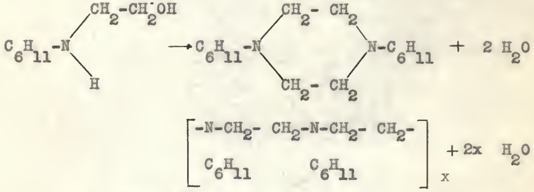
A study was made, by Birkofer (25), to determine the influence of the residue on the nitrogen atom upon catalytic debenzylation. He carried out hydrogenations at room temperature and at atmospheric pressure in ethanol or acetic acid using palladium oxide or platinum oxide as catalyst. Birkofer found that 1, 4-dibenzylpiperazine in acetic acid gives a ninety-two per-cent yield of piperazine diacetate when palladium oxide was used as the catalyst.

Chitwood and McNamee (63) found that piperazinopiperazine could be obtained by reacting glyoxal with excess ethene diamide or substituted ethene diamines, such as; propylene diamine in alcohol or water as solvent. In a patent, recently assigned to Carbide and Carbon, Chitwood (64) found that 1-, 2-, 3-, and 4-substituted piperazine compounds could be obtained by hydrogenating piperazinopiperazine compounds. The hydrogenation was carried out in liquid-phase in the presence of a catalyst; nickel, copper, pallasium etc., around 90°. By this method there may be prepared 1, 4-dibutylpiperazine from N, N', N'', N'''-tetrabutyl piperazinopiperazine. In a similar manner piperazines substituted in 2- or 3- position, e. g., 2-methylpiperazine, can be prepared.

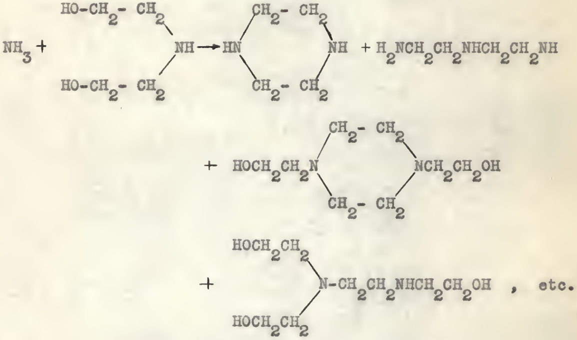
2. Discussion

There are many methods known for the production of piperazine but most of them are impractical for commercial production. Of the few syntheses that are carried out on a commercial scale, most of them have numerous disadvantages. The catalytic method of alkylation of amines with alcohols appears to be of sufficient importance to warrent a patent application by Kitchen and Pollard (171). This method is a new and useful method of synthesizing piperazine whereby the anhydrous material can be conveniently obtained.

The piperazines previously prepared were synthesized mainly from amines and amino-alcohols. In the case of each ring closure, two molecules of the amine or amino-alcohol were involved, and two molecules of water were split out as the result of ring closure. Either a diethanolamine reacted with a primary amine or two molecules of the diethanol amine type reacted to form a piperazine ring with the splitting off of two molecules of water. From this type of reaction, there is a possibility of many side reactions. This tendency is reduced and there remains only the possibility of linear polymer formation, as a side reaction, when the nitrogen atom already is partially substituted. This advantage is illustrated by N-cyclohexylethanolamine which cyclizes to form 1, 4-dicyclohexylpiperazine.

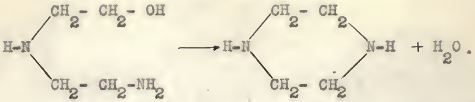


When the dehydrogenation reaction, as applied by Poppenberg, is applied to the synthesis of piperazine itself, it is apparent that many side reactions are possible by bimolecular reaction. This leads to many linear and branched-chain polymers that are undesirable.



This type of reaction is undesirable because ammonia is less reactive toward alkylation than is a primary or secondary amine.

It is apparent that the optimum reaction would be an intramolecular dehydrogenation, in which only one molecule of water is removed per molecule of piperazine formed. By this method of synthesis, it is apparent that side reactions are brought to a minimum. Because of this fact, the compound N-(B-hydroxyethyl)ethene diamine was selected for the starting material in the works of Kitchen (124) and Goulding (104).



The starting material in the work of Kitchen and Goulding is available from Carbide and Carbon in commercial quantities. There has been little demand for this material in the past, but since its ideal qualities have been demonstrated for the synthesis of piperazine, it may be in more demand in the future. While there has been no great technical demand for this material, it is available in considerable amounts as a by-product, formed during the manufacture of ethene diamine, diethene triamine and other polyethene polyamines. In the event that this material should ever be available in inadequate amounts, it can be readily synthesized by alkylating ethene diamine with ethene oxide (124, 126). Ethene diamine is available in high yields from the ethene-chloride-ammonia reaction, and larger amounts are available as a by-product in the manufacture of ethene chlorohydrin.

3. Catalytic Alkylation Method

The present investigation of catalytic vaphor-phase alkylation was prompted by the results of other investigators. The vapor-phase alkylation of aromatic amines with alcohols has been investigated by Maihle and de Godon (144), Brown and Reid (32), and by Shuikin and co-workers (195, 197).

They obtained high yields and found that effective catalysts were oxides of aluminum, titanium, iron and silica gel. The simultaneous dehydration of ethanol and ammonia, using alumina catalyst have been reported by Shuikin and co-workers (196).

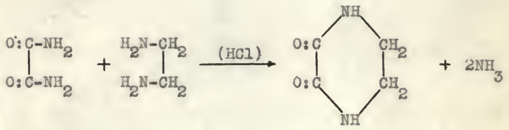
The formation of benzylphenylamine by the alkylation of phenylethyl amine with benzyl alcohol, in the presence of palladium catalyst, by Kindler and co-workers (123). The alkylation of primary and secondary amine with alcohols by the use of copper-chromium oxide catalyst, have been reported by Adkin and co-workers (109, 166, 193). The use of nickel as a catalyst has also been investigated (6a, 193, 233a). Bain and Pollard (16, 17, 18) have applied this method to the preparation of piperazine derivatives from amines and amino-alcohols (171).

4. 2, 3-diketopiperazine

The work of Aspinall (10) demonstrated a method of preparing monoketopiperazine. The ease and yield of this synthesis appeared to point out a method in which 2, 3-diketopiperazine could be prepared by reacting ethylene diamine with diethyl exylate. Hofmann (111) investigated the reaction between ethylene diamine and diethyl exylate and found that 2, 3-diketopiperazine could be prepared by this method. In order to determine the yield of 2, 3-diketopiperazine, the author performed the Hofmann synthesis and found that a maximum yield of about one per-cent could be obtained under favorable conditions. Another synthesis of 2, 3-diketopiperazine was carried out by van Alphen (224) using a different method of reacting diethyl exalate with ethylene diamine. The synthesis of van Alphen required approximately four weeks for completion of the reaction. The yield was very poor, due to side reactions. In light of the previous efforts to prepare 2, 3-diketopiperazine, another effort has been made to synthesize this long known compound. The present method consists of reacting anhydrous ethylene diamine, in anhydrous 1, 4-dioxane, with oxamide.
EXPERIMENTAL: - Sixty-three grams of finely powdered oxamide was placed in a three necked flask. The three-necked flask was fitted with an electric stirrer, reflux condenser, and an electric heater. Sixty grams of ethylene diamine con-

tained in two hundred and fifty milliliters of anhydrous 1, 4-dioxane was then poured into the three-necked flask with the finely powered oxamide. Two milliliters of concentrated hydrochloric acid was added as a catalytic agent.

The mixture was heated to reflux temperature with vigorous stirring. The stirring was accomplished by means of a collapsible stainless steel stirrer which swept the sides of the flask. The reflux temperature with stirring was continued for twenty-four hours or until ammonia was no longer evolved.



The finely divided oxamide, suspended in the 1, 4-dioxane ethylene diamine mixture, slowly formed a yellowish amorphous substance that had a tendency to stick to the sides of the flask and stirrer. If the reacting mixture is not stirred vigorously and the material swept from the sides of the flask, charring of the material becomes evident. There is no evidence of charring on the stainless steel stirrer.

When ammonia was no longer evolved, the heating was stopped and the flask cooled. The cooled mixture had a large amount of solid material that had to be broken up to remove it from the three-necked flask. The entire mixture was poured out of the flask into a beaker. The solvent, 1, 4-dioxane, was removed from the solid material by filtering on a Buchner funnel. The solvent was evaporated in vacuo and the solid material combined with the material in the funnel.

The solid material formed in the reaction was masserated in several liters of boiling water. The hot water extract was filtered on a hot Buchner funnel. The filtrate contained the 2, 3-diketopiperazine. When one-tenth of the filtrates was evaporated, a dark colored crystaline precipitate appeared. This material was filtered out on a Buchner funnel. This material, light brown in color, had no melting point and charred somewhere above 350°. Since there was only a very small quantity of this material, no further work was done on this product. It is thought, however, that this material may be some condensation product of 2, 3-diketopiperazine.

The above filtrate was evaporated to one-tenth of its original volume. A light cream colored precipitate appeared that was only soluble in boiling water. The color of this material is white with a faint cream colored cast when dry. The dried product had a decomposition point of 285°. On slow heating the white material changed to a brick red substance around 135° and did not melt below 350°. This compound charrs around 425° (uncorr.). When the copper block melting point apparatus was heated to 275° and the melting point tube containing the white product put into it, the white material decomposed at 285°.

The theoretical yield of 2, 3-diketopiperazine is 81.6 grams.

A yield of 41.1 grams of material melting at 285° was obtained.

The per-cent yield of 2, 3-diketopiperazine is 50.3.

Melting point of 2, 3-diketopiperazine:	M.p. 285°(dec.)(224)
Melting point of reaction material:	M.p. 285°(dec.)
Melting point of 1, 4-dinitro-2, 3-diketopiperazine:	M.p. 150°(dec.)(224)
Melting point of 1, 4-dinitro derivative of material:	M.p. 150°(dec.)

5. Nickel Palmetate

Two hundred and fifty-six and a half grams of palmetic acid is melted in one liter of distilled water at 100°. A saturated solution of potassium hydroxide, containing forty-five grams, is slowly mixed with the melted palmetic acid. This mixture is mixed with heating until completely saponified. The saponified mixture is then filtered on a Buchner funnel to remove solid suspended material.

One hundred and forty-five grams of nickelous nitrate is dissolved in one and a half liters of distilled water and then added to the solution of sodium palmetate with agitation. When the reaction is completed, the precipitate is allowed to settle. The precipitate is washed three times by decanting and then filtered on a Buchner funnel.

The precipitate is then washed with two hundred milliliters of ethanol to remove the excess palmetic acid, and then air dried to constant weight. The air dried nickel palmetate is then mixed with six per-cent of its weight of purified palmetic acid in a morter.

The free palmetic acid is added to act as a binder in the preparation of catalyst in the pellet form.

The inorganic analysis of impurities in the nickel palmetate is:

cobalt	0.10%	lead	0.005%
copper	0.02%	zinc	0.050%
iron	0.01%		

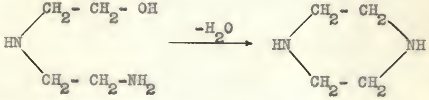
C. EXPERIMENTAL

1. Introduction

The following experimental work was undertaken, in the syntheses of pyrazine and piperazine, to show that a continuous vapor-phase process for simultaneous ring closure and dehydrogenation of N-(B-hydroxyethyl)ethene diamine could be performed at reduced pressures.

In order to accomplish the vapor-phase syntheses of pyrazine and piperazine, it was found that a new type of apparatus had to be constructed which would give the required performance. The requirements of such an apparatus were that it keep the vaporized material under constant control at all times and maintain the various temperatures at the desired points. With this apparatus, described later, all of the requirements for successful operation were accomplished.

The starting material, for the syntheses of pyrazine and piperazine, is N-(B-hydroxyethyl)ethene diamine. It is thought that the first reaction is one of dehydration of the molecule to give the 1, 4-heterocyclic compound, piperazine.



The next reaction is thought to be one of dehydrogenation of the piperazine molecule to give pyrazine.

Since the dehydrogenation product, pyrazine, was the desired end-product, the catalysts were selected with the idea of obtaining maximum yields of pyrazine. It was found, however, that in almost every case, piperazine was produced in greater quantities at 300° and 400°, whereas, pyrazine was always produced as the major product at 200°.

There was very little evidence of molecular decomposition in the control run at 200°, without a catalyst. In the experimental control runs at 300° and 400° at 50 mm. pressure, large amounts of carbon and decomposition products were formed. No pyrazine or piperazine was found in the control runs at 200°, 300° or 400°; but ethene diamine, ethanol and ethanol amine were found in the condensate of the vapors. This indicates that molecular fission and molecular decomposition occurred without molecular rearrangement when no catalysts were used in the reaction tube. These products were also found in the experimental runs with all catalysts.

An attempt was made to find an explanation for the molecular fission, dehydration and dehydrogenation by the method presented by Whitmore (230a). This attempt was abandoned because of lack of evidence that would support the theories of Whitmore. Additional work, however, is anticipated on this phase of catalytic vapor-phase reactions.

2. Equipment

The apparatus, Plate 1., for the catalytic vapor-phase synthesis of piperazine and pyrazine is unique in design and operation. The apparatus is designed to run at either reduced pressures or at atmospheric pressure. All of the present work, however, is run at reduced pressures. The design permits liquifiable solids, such as piperazine, as well as liquids to be subjected to vapor-phase reactions. All heating is accomplished by electric heaters.

The apparatus shown in Plate 1. consists of seven pieces: 1. a preheater or melting tube, 2. a drop counter, 3. a vaporizing flask, 4. the catalytic reaction tube, 5. a condensing head, 6. a thermopile, 7. an expansion condenser and vapor trap.

1. The preheating or melting tube consists of a graduated tube, twelve inches in length, with a 4 mm. stopcock at the bottom and attached to a No. 20 standard taper. The top of the preheater has a No. 25 standard taper that can be fitted with a standard taper plug which has a 2 mm. stopcock attached.

2. The drop counter consists of a female No. 20 standard taper connected to a male No. 20 standard taper. A drip-point is formed at the junction of the two standard tapers to allow timing of the drops from the preheater.

3. The vaporizing flask consists of a 200 ml. round bottom flask which has two standard taper connections.

The standard taper joints are a No. 20 and the other a No. 25 whose axes form a 45° angle.

4. The catalytic reaction tube is fitted with a male No. 25 standard taper at the junction with the vaporizing flask and with a female No. 25 at the junction of the condensing head. The reaction tube is of "Vicor" glass combustion tube stock, 20 inches long and 1 inch in diameter.

5. The condensing head is of novel design. It has a cold finger condenser, connected to the condensing head by means of a standard taper connection, that can be readily removed for cleaning purposes, as shown in Plate 1.

6. The thermopile is constructed of iron-constantan duplex glass covered lead wire of No. 30 B. & S. gauge. The iron-constantan lead wire is obtained from Leeds and Northrup Co. The method of construction and recommendations for thermopiles, as given by Wood and Cork (242), is followed for the construction of the iron-constantan thermopile. The thermopile is calibrated against a standardized thermometer. A Hoskins type PA indicating pyrometer is used in conjunction with the thermopile.

7. The expansion condenser and vapor trap, not shown in Plate 1., consists of three concentric tubes. The inner tube and the tube on the outside are connected together and ice water, at 0°, is circulated through them. The expansion condenser is connected to a vapor trap by means of a No. 30 standard taper. The vapor trap is immersed in an ice-hydro-

Plate No. 1

chloric acid mixture contained in a Dewar flask for cooling.

The preheating or melting tube is heated by a spiral heating element which is stretched longitudinally outside of the preheating tube and enclosed within a glass jacket.

The vaporizing flask is heated by a hemispherical heating unit that surrounds the lower half of the flask.

The catalytic reaction tube is heated by a clam-type heater which is constructed from ceramic refractories obtained from Fischer Scientific Company. The refractories are held together with a hinged angle-iron frame. A pair of heating elements, having a total resistance of 39.2 ohms, were placed inside of the refractories. The heating elements are connected with a series of matched slide resistances as shown in Figure 1. The heating elements, H_1 and H_2, are made of Nichrome resistance wire. Each heating element has 19.6 ohms resistance. The slide resistances, R_1, R_2, R_3 and R_4, are matched variable slide resistances. Each slide resistance has a capacity of 8.6 amperes and 5.7 ohms resistance. The circle in Figure 1. containing the letters 1L, 2, 3, and 4 designate a General Electric three heat switch. When the G. E. switch is on "medium", only one heating element is heating. When the G. E. switch is on "high" both heating elements, H_1 and H_2, are in parallel and the variable slide resistances, R_1 and R_2, are in parallel and variable slide resistances R_3 and R_4 are in parallel.

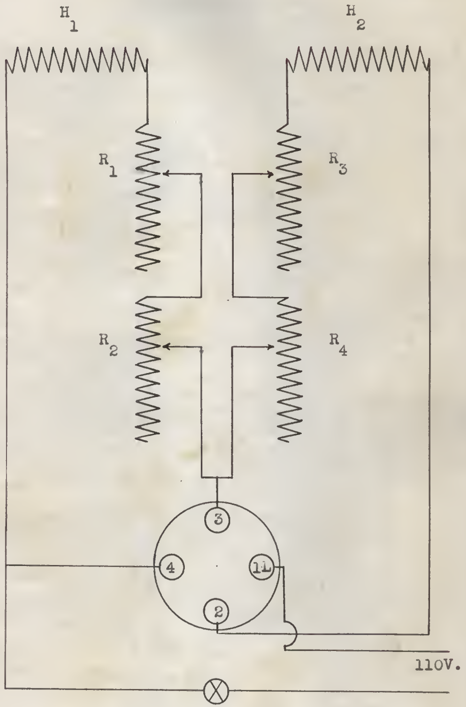


Figure No. 1

When the G. E. switch is on low both heating elements, H_1 and H_2, are in series and the variable slide resistances R_1, R_2, R_3 and R_4 are in series. When additional voltage regulation is required a 15 ampere-8.8 ohm variable resistance is inserted at the point designated by a circle X.

It was found, however, that the temperature could be more easily controlled if an eighteen ampere variable voltage transformer, manufactured by American Instrument Company, were used instead of the slide resistances. When using the variable voltage transformer, the temperature could easily be controlled to within a two degree range.

To set up the apparatus for the catalytic vapor-phase reactions, the following procedure was used. The reaction tube was filled with short glass Rauschig-rings to a depth of five inches. The thermopile sheath was then rested on the Rauschig-rings and held in the center of the reaction tube. The prepared catalyst, of known surface area, was then poured into the reaction tube around the thermopile sheath. A Witt filter disc, with a hole large enough to slip over the thermopile sheath was then placed in the reaction tube to hold the catalyst in place.

All of the standard taper connections were coated with a thin smooth coating of graphite before coating them with hot vacuum sealing compound.

The reaction tube was then inserted into the corresponding standard taper in the vaporizing flask. The standard tapers on the drop counter were treated in a similar manner and inserted into the vaporizing flask. The preheating tube was then fitted into the drop counter. The condensing head, containing the cold-finger condenser, was then fitted to the reaction tube. A standard taper closure was fitted into the back side of the condensing head which sealed the thermopile sheath.

The assembled apparatus is then clamped into the clam-type heater contained on an iron frame, as shown in Plate 1. The thermopile is inserted into its sheath and then connected to the indicating pyrometer. The vacuum outlet on the condensing head is connected to the expansion condenser. The vacuum outlet on the vapor trap is then connected to a Zimmerman mercury gauge which allowed the pressure to be measured to one-tenth of a millimeter.

The pressure is accurately controlled by a sulfuric acid manostat of the Hershberg-Huntress type (107a) that was connected to the Zimmerman gauge. The manostat is in turn connected to a vacuum pump. The action of the vacuum pump on the manostat can be checked by partially closing a stopcock placed between the pump and the manostat. Fluctuation is minimized by placing a five gallon bottle between the manostat and the system.

The parts of the apparatus through which vapor passes are covered with several layers of glass wool. This is necessary to prevent excessive loss of heat and to insure uniform heating of the apparatus. The vaporizing flask is heated to approximately 100° above the boiling point, of the N-(B-hydroxyethyl)ethene diamine, at the pressure of operation. This is necessary to maintain immediate vaporizing of all material entering the vaporizing flask and to insure a uniform flow of vapor through the reaction tube.

The catalyst, whose composition is shown later, is pelleted in a die made for this purpose; shown in Figure 2. The catalytic material in powder form is poured into the die and the powder pressed into quarter-inch tablets on a hydraulic press. The tablets, as produced in the pelleting die, are then quartered with a sharp knife before using in the reaction tube. The volume of the catalyst is determined by the conventional liquid displacement method.

The operation of the apparatus is very simply carried out. The stopcock at the bottom of the preheating tube is shut off and the desired number of grams of N-(B-hydroxyethyl)ethene diamine is poured into the preheater which is maintained at 100° at atmospheric pressure. The vacuum is started and the desired pressure is accomplished by the proper adjustment of the manostat. The cold finger condenser in the condensing head and the expansion condenser are connected in series and cold water, at 0°, is first circulated through the expansion condenser and then through the cold finger condenser before returning to the cold water reservoir. As the vapor passes, through the reaction tube,

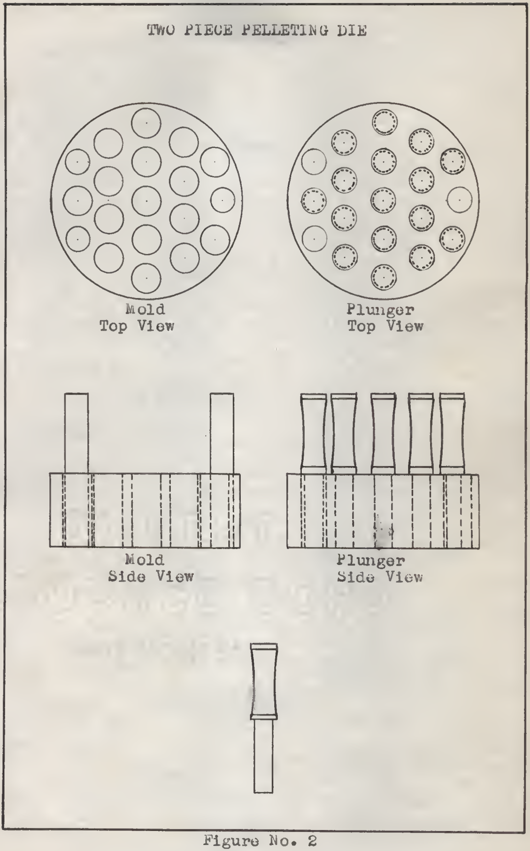

TWO PIECE PELLETING DIE
Mold
Top View
Plunger
Top View
Mold
Side View
Plunger
Side View

Figure No. 2

into the condensing head, it comes into contact with the cold finger condenser which condenses the vapor to a liquid. The liquid is caught in a receiving flask as shown in Plate 1.

The reacted mixture is fractionated by distilling through a 15 inch column packed with quarter-inch Berl saddles and provided with a Hopkins type condenser. The condenser was designed for the distillation of solids, being fitted to the distillation head by a standard taper connection. Thus it could be removed from the head when it is desired to scrape off any adhering piperazine. The condenser was provided with an off-set drip-point so that the amount of reflux could be regulated a certain amount by rotating the condenser in its standard taper connection.

The distilling column is provided with an electrically-heated jacket. In all cases the distilling flask was heated by an electrical heater which minimized bumping by even heat distribution on the lower hemispherical surface of the flask. This type of heating made it possible to avoid super-heating the contents of the distilling flask and minimized decomposition.

3(a). Experimental Procedure

The following experiment is described in detail, to exemplify the experimental conditions used in the vapor-phase experiments. Since a series of experiments, were run on eight different catalysts, the results of the experiments are divided into eight groups. Each group contains introductory information on the type and composition of catalyst, tables of experimental conditions and yields of piperazine and pyrazine, and observations.

When the catalyst is placed in the vapor-phase apparatus, it is calcined by heating the catalyst to 200° and passing hot air over the catalyst for 72 hours. This procedure oxidized all of the organic material used as a binder and lubricant in the preparation of the catalyst.

After the calcining has been completed, the preheater and vaporizing flask are heated to 100° and 235° respectively. The cold water is started circulating through the expansion condenser and condensing head. The vapor trap is immersed in an ice-hydrochloric acid mixture. The cold end of the thermopile is immersed in crushed ice containing enough water to give slight fluidity.

When all temperatures are at the desired points and all cooling areas sufficiently chilled, the vacuum is regulated at 50 mm. pressure. Then 104.2 grams of N-(B-hydroxyethyl)ethene diamine is placed in the preheater and allowed to come to 100° -125°. The N-(B-hydroxyethyl)ethene diamine is then allowed to drop into the vaporizing flask at the rate of one drop per second. The timing of the reaction is started as soon as condensed material appears in the condensing head and is stopped 1.25 hours later when the last drop of condensate appears.

The amount of condensate is weighed in a tared flask to determine the amount of loss due to carbonization. This information, visual appearance of the catalyst, and the time required to recalcine the catalyst is used to determine the condition of the catalyst.

The reacted material is washed into a 500 ml. flask with 250 ml. of benzene-ethanol azeotrope, boiling point 68.25°, and then subjected to fractionation on the 15 inch column previously described. At the beginning of the distillation, there was a tendency for the liquid to bump due to slight super-heating which disappeared in a few minutes. The first distillate boiled at 60°, having a cloudy appearance which separated into two layers on cooling. The boiling point then rose to 64.85°, the boiling point of the ternary constant boiling mixture containing 74.1 per-cent benzene, 18.5 per-cent ethanol, and 7.4 per-cent water. When most of the water had distilled over in the azeotropic mixture, the boiling point gradually rose to 68,25° when the anhydrous benzene-ethanol azeotrope distilled over. After the anhydrous benzene-ethanol azeotrope had been removed, the temperature rose from 78° to 81° where the ethanol and benzene distilled over. When all of the benzene and ethanol had been removed, the temperature rose rapidly to 113°. The receiver was changed and the fraction boiling at 113° to 125° was collected. The temperature then rose rapidly to 140° and the receiver was changed and anhydrous piperazine was collected, boiling mainly between 140° and 150°. The residue is a viscous brown liquid. During the distillation of the piperazine it was necessary to keep the piperazine melted as it flowed from the distilling head into the receiver because of the tendency of the product to solidify.

The fraction boiling at 113° to 125° was placed in a separatory funnel with 10.0 ml. of saturated potassium hydroxide and the mixture was then extracted with 200 ml. of ether. The ternary constant boiling mixture was made acid with a few drops of concentrated hydrochloric acid and then an excess of saturated mercuric chloride was added to it. A white precipitate formed immediately. This precipitate was filtered out and placed in an Erlenmeyer flask containing an excess of saturated potassium hydroxide. The potassium hydroxide solution was extracted with ether. The ether extracts were combined and cooled to 0°, and then evaporated in vacuo at 0°. The solid residue was taken up with absolute ethanol and distilled on a semimicro distilling column to give the anhydrous pyrazine boiling at 115.8° to 116.3° at 760.5 mm. pressure.

It was found that excessive losses of pyrazine occurred in the distillation of anhydrous pyrazine so two runs were made under similar experimental conditions. The two runs were treated as in the method above with the exception that in one run, instead of distilling the anhydrous pyrazine, it was converted into the mercuric chloride derivative. The per-cent pyrazine was calculated from the mercuric derivative and compared with the yield of anhydrous pyrazine obtained by distillation. A 12.0 per-cent loss of pyrazine was found to occur in the distillation of the pyrazine-ethanol mixture. Since the amount of anhydrous pyrazine obtained by distillation did not represent the correct amount of pyrazine formed in the reaction, the yields of pyrazine were corrected by 12.0 per-cent.

A small trace of acetaldehyde was found in the ternary benzene-ethanol-water solution. No attempt was made to make quantitative determinations of this product because it was so small and a by-product.

3(b). Examples of Calculations

The volume of vapor passing through the reaction tube is determined by the formula, $PV = \frac{g}{m} R\ T$. The data taken from table II, line 4 is:

$P = 50$ mm. $\quad$ M.W. $= 104.2$ $\quad$ $R = 0.082$

$V = ?$ $\quad$ g. $= 94.6$ $\quad$ $T = 400^\circ$

$V = (760)(50^{-1})(0.082)(94.6)(104.2^{-1})(673) = 761.5$ liters

Marek and Hahn (138a) define Space Velocity as the volume of reacting gas, measured at normal temperature and pressure, passed in contact with unit volume of the catalyst per hour. The velocity of vapor reacted under operating conditions is first determined.

Time = 90 minutes $\quad$ Volume of catalyst = 20 ml.

Volume of gas = 761.5 liters

velocity of vapor = (volume) (hours^{-1}) $(\text{volume of catalyst}^{-1})$

velocity of vapor = $(761.5)(60)(90^{-1})(20^{-1}) = 25.38$ liters-ml.$^{-1}$-hrs.$^{-1}$

The velocity of vapor per hour is then converted to Space Velocity at normal temperature and pressure by the formula $\frac{PV}{T} = \frac{P'V'}{T'}$, where

$P = 50$ mm. $\quad$ $P' = 760$ mm.

$V = 25.38$ liters -ml.$^{-1}$-hr.$^{-1}$ $\quad$ $V' = ?$

$T = 673^\circ$ $\quad$ $T' = 273^\circ$

$\frac{25.38 \times 50}{673} = \frac{760 \times V'}{273}$;$V' = 0.677$ liters-hrs.$^{-1}$-ml.$^{-1}$ at NTP

According to the definition of Marek and Hahn, the Space Velocity is 0.677 liters per ml. per hour.

In the reaction, 94.6 grams of the N-(B-hydroxyethyl) ethene diamine gave 2.0 grams of pyrazine and 4.5 grams of piperazine. The calculation for the per-cent yield of pyrazine follows:

$\frac{94.6 \times 80}{104.2} = X$; $X = 72.6$ grams theoretical yield of pyrazine

$\frac{2.0}{72.6} \times 100 = 2.8$ per-cent yield of pyrazine

Since piperazine was also obtained in the reaction, the number of grams of N-(B-hydroxyethyl)ethene diamine required to make 2.0 grams of pyrazine is found by the following calculations:

$\frac{2.0 \times 104.2}{80} = X$; $X = 2.9$ grams of N-(B-hydroxyethyl) ethene diamine required to make 2.0 grams of pyrazine.

The number of grams of N-(B-hydroxyethyl)ethene diamine required to make 2.0 grams of pyrazine is then subtracted from the original number of grams of N-(B-hydroxyethyl)ethene diamine and the following calculation made to calculate the theoretical amount of piperazine.

$\frac{94.9 - 2.9}{104.2} = \frac{X}{86}$; $X = 78.7$ grams theoretical yield of piperazine.

The per-cent yield of piperazine is obtained by the following calculation: $\frac{4.5}{78.7} \times 100 = 6.0$ per-cent yield of piperazine.

3(c). GROUP ONE

Catalyst No. 1

Introduction

Many publications have appeared which state that the method of preparing catalysts influence the catalytic activity of the catalyst. The catalyst used in the following group of experiments was prepared in the following way:

Sixty grams of silicic acid is dissolved in 100 ml. of warm saturated hydroxide. The resulting sodium silicate solution is then filtered on a Buchner funnel having an asbestos mat to remove all insoluble material. The resulting sodium silicate solution is clear and transparent.

One hundred grams of sodium tungstate is dissolved in 200 ml. of boiling water. The hot solution of sodium tungstate is then poured into the warm solution of sodium silicate. The mixing of the sodium silicate- sodium tungstate solution is carried out by means of an electric motor stirrer that agitates the mixture violently.

The resulting mixture is acidified with 2.0 normal nitric acid which contains 0.1 per-cent of nickel nitrate. The acid is added very slowly with violent agitation. After each addition of acid the mixture is agitated until the coagulated material is dissolved. This procedure is continued until all excess alkali is neutralized.

As the addition of acid is continued, the solution takes on a yellow color which masks the blue-green color of the dissolved nickel nitrate. The solution becomes more cloudy as the addition of acid is continued and frequent outside indicator tests are made to determine the point at which the solution becomes acid. At the point when the solution becomes acid, a bright violet cast appears in the light yellow opaque solution. A small addition of excess nitric acid is made to remove this color and to help precipitate the gel that is formed. At this point, the agitation is stopped and the precipitate is allowed to settle. Throughout the mixing and acidification, no heat is applied to the reaction.

The precipitate is filtered on a Buchner funnel and then air dried. After the precipitate is dried to constant weight in the drying oven at 80°, enough nickel palmetate is added to make a 5.0 per-cent mixture. The mixture is then thoroughly ground in a stone mortar. The moisture is then adjusted to 1.0 per-cent for pelleting.

The catalyst is pelleted at 1800 pounds per square inch.

Observations

An excessive amount of ethene diamine was found in every run which necessitated the extraction of the pyrazine fraction with ether to remove the pyrazine from the ethene diamine.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 0.5 g.: 1 g. at 200° and 50 mm.

ethene diamine: pyrazine:: 1.0 g.: 1 g. at 300° and 50 mm.
ethene diamine: pyrazine:: 1.2 g.: 1 g. at 400° and 50 mm.

Other products were formed in the reaction. These products were acetaldehyde, ethylamine, ethyl aminoethanol, and ethanol.

2, 4-dinitrophenylhydrazone of acetaldehyde	M.p. 168.5°
2, 4-dinitrophenylhydrazone of aldehyde in reaction	M.p. 168.5°
mixed melting point of the two derivatives	M.p. 167° - 169°
Hydrochloride of ethylamine	M.p. 108°

This melting point duplicates the melting point in the literature.

No ethylamine was available for a derivative.

Hydrochloride of ethene diamine	M.p. 325°(dec.)
Hydrochloride of amine from reaction	M.p. 325°(dec.)
Mixed melting point of the two derivatives	M.p. 325°(dec.)
Gold chloride derivative of ethyl aminoethanol	M.p.127°(dec.)
Gold chloride derivative of alcohol amine from reaction	M.p. 127°(dec.)
Mixed melting point of the two derivatives	M.p. 126°(dec.)
Ethyl N-(a-naphthyl) carbamate	M.p. 79°
N-(a-naphthyl) carbamate of alcohol in reaction	M.p. 78°
Mixed melting point of the two derivatives	M.p. 78 °-79°

The Spectrographic Analysis of Catalyst No. 1.

The following data are qualitative analyses, with only rough estimates of concentrations present. No attempt was made to get quantitative values. Each value should be interpreted as indicating only an order or magnitude and may be in error by a factor of three or more.

Non-detection of an element is indicated by a dash (——), in the table. This does not necessarily mean that the element is absent from the catalyst, but only that, if present, it occurs in a concentration below the lower limit of detection.

"N.A." indicates "no analysis was run for this element".

> indicates "greater than".

>> indicates "much greater than".

∠ indicates "less than".

Approximate lower limit of detection		Catalyst No. 1	Approximate lower limit of detection		Catalyst No.1
Tl	0.1 %	— %	Al	0.001 %	0.005 %
Sr	0.0005	—	Co	0.001	(3)
Li	0.001	—	Ni	0.001	>0.1
Rb	0.05	—	Ag	0.0005	—
K	0.005	0.05	Cu	0.0005	0.0005
Na	—	0.2	Cd	0.01	(4)
Ca	—	0.1	Ti	0.001	0.01
Mg	—	0.01	Mo	0.001	0.10
Si	—		Be	0.001	—
Ba	0.0005	0.001	Bi	0.01	—
Fe	0.001	0.1	Sb	0.05	—
V	0.005	—	As	0.5	—
Y	0.01	—	Sn	0.001	N.A.
Cr	0.001	(1)	Pb	0.001	0.005
Mn	0.001	(2)	Ge	0.001	—
W	0.1	>>0.1	Im	0.001	—

Table No. I

(1) Tungsten interferes with detection of chromium but the latter element, if present in this catalyst, is not present in quantity much more than 0.001 per-cent.

(2) Manganese, if present in this catalyst, is in a concentration less than 0.005 per-cent.

(3) The presence of cobalt is doubtful in this catalyst. If present, it is in concentration less than 0.001 per-cent.

(4) Vanadium interferes with the detection of cadmium. The latter, if present in this catalyst, is not present in concentration greater than about 0.05 per-cent.

Table No. II

Experimental Data for Catalyst Number 1.

Temperature degrees Centigrade	Time in hours	Pressure in milli-meters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
200	1.25	50	103.5	23.42	0.89	-	79.4	2.4	3.1	trace	---	---	93.2
200	1.50	50	98.5	18.58	0.71	-+?	75.6	3.1	4.1	trace	---	---	75.1
200	2.75	50	102.8	10.57	0.41	-+?	78.9	5.8	7.4	trace	---	---	86.0
200	5.00	100	81.6	2.31	0.18	++++	62.7	2.6	4.1	1.0	64.5	1.6	65.5
200	2.00	150	92.5	4.36	0.49	+++	71.1	2.6	3.7	0.5	73.5	0.7	63.0
200	2.00	200	85.2	3.01	0.46	+++	65.4	1.7	2.6	0.5	68.5	0.7	78.6

1. Negative(-) indicates slight reduction.+? Indicates doubtful carbonization. +Indicates slight carbonization. ++Indicates noticable carbonization.+++Indicates most of surface area carbonized.++++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72

Table No. III

Experimental Data for Catalyst Number 1.

Temperature degrees Centigrade	Time in hours	Pressure in millimeters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
300	1.00	50	106.9	36.63	1.15	-	82.0	2.3	2.8	trace	---	---	98.7
300	1.50	50	98.3	22.46	0.70	+	75.3	3.0	3.9	trace	---	---	72.4
300	2.25	50	97.3	14.82	0.46	++	74.6	4.8	6.5	trace	---	---	57.8
400	1.50	50	94.6	25.39	0.63	++++	72.6	2.0	2.8	4.5	75.7	6.0	65.5
400	2.25	50	93.2	22.53	0.60	++++	71.6	2.2	3.0	4.6	74.6	6.2	62.8
400	3.50	50	83.3	12.95	0.35	++++	63.9	3.3	5.2	5.9	65.2	9.0	38.8

1. Negative(-) indicates slight reduction.+? Indicates doubtful carbonization. +Indicates slight carbonization. ++Indicates noticable carbonization.+++Indicates most of surface area carbonized.++++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

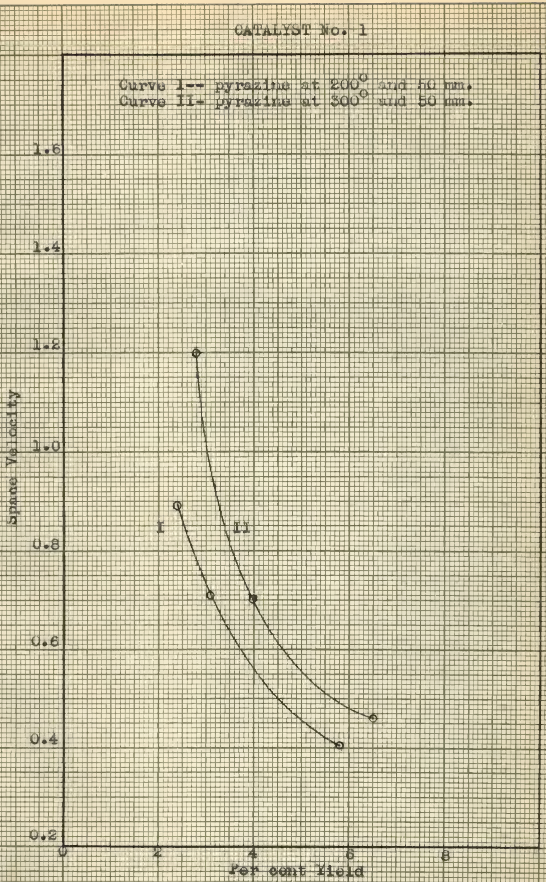

CATALYST No. 1
Curve I-- pyrazine at 200° and 50 mm.
Curve II- pyrazine at 300° and 50 mm.
Space Velocity
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
I
II
0
2
4
6
8
Per cent Yield

Figure No. 5

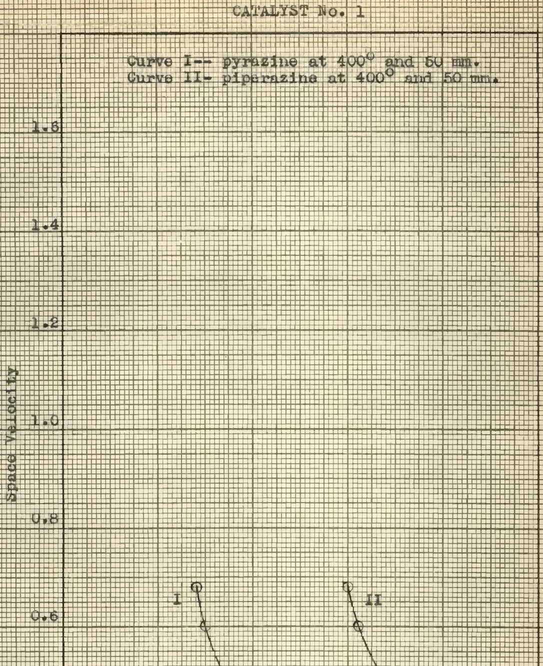

CATALYST No. 1
Curve I-- pyrazine at 400° and 50 mm.
Curve II- piperazine at 400° and 50 mm.
Space Velocity
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
I
II
0
2
4
6
8
Per cent Yield

Figure No. 4

3(d). GROUP TWO

Catalyst No. 2-R

Introduction

The catalyst used in these experiments was prepared in the following manner.

Two hundred grams of silicic acid (2.081 moles) was added to 133.2 grams of molybdic acid (0.822 moles). The mixture is ground together in a mortar. When the mixture was thoroughly ground together, 16.0 grams of nickelous palmetate, containing 6.0 per-cent free palmetic acid, was then ground into the mixture in a stone mortar. Forty-three and one-half grams of distilled water was added to make the correct moisture content for pelleting.

The catalyst is then pelleted at 1200 pounds per square inch.

Observations

The catalyst is charred to a +4 in the first few minutes of the 200° run at 50 mm. pressure. It was necessary to calcine the catalyst for 48 to 72 hours at 400° between each run to remove the carbon from the catalyst.

Ammonia with ethylamine is given off rapidly for the first few minutes of each run, until a black deposit forms on the catalyst.

Ethene diamine is found in large amounts in every run. This necessitated the extraction of the pyrazine fraction with ether to separate the pyrazine from the ethene diamine.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 2 : 1 at 200° and 50 mm.
ethene diamine: pyrazine:: 2 : 1 at 300° and 50 mm.
ethene diamine: pyrazine:: 2 : 1 at 400° and 50 mm.

Other products found in the reacted mixture are: acetaldehyde, ethyl aminoethanol, ethylamine. These products were identified by the same derivatives used in the identification of these products in group one.

Spectrographic Analysis of Catalyst No. 2-R

The following data are qualitative analyses, with only rough estimations of concentrations present. No attempt was made to get quantitative values. Each value should be interpreted as indicating only an order of magnitude, and may be in error by a factor of three or more.

Non-detection of an element is indicated by a dash (——). in the Table IV. This does not necessarily mean that the element was absent from the catalyst, but only that, if present, it occurrs in a concentration below the lower limit of detection.. Values for the approximate lower limit of detection are given for each element in the Table IV.

"N.A." indicates "no analysis was run for this element".

$>$ indicates "greater than".

$\gg$ indicates "much greater than".

$<$ indicates "less than".

Approximate lower limit of detection	Catalyst No.2-R	Approximate lower limit of detection	Catalyst No.2-R
Tl 0.1 %	——— %	Al 0.001 %	——— %
Sr 0.0005	———	Co 0.001	(1)
Li 0.001	———	Ni 0.001	> 0.1
Rb 0.05	———	Ag 0.0005	———
K 0.005	———	Cu 0.0005	(2)
Na ———	0.01	Cd 0.01	(3)
Ca ———	0.05	Ti 0.001	0.01
Mg ———	0.01	Mo 0.001	>>0.1
Si ———	(5)	Be 0.001	———
Ba 0.0005	———	Bi 0.01	(4)
Fe 0.001	0.1	Sb 0.05	———
V 0.005	———	As 0.5	N.A.
Y 0.01	———	Sn 0.001	N.A.
Cr 0.001	< 0.001	Pb 0.001	0.001
Mn 0.001	———	Ge 0.001	———
W 0.1	———	In 0.001	———

Table No. IV

(1) The presence of cobalt in this catalyst is doubtful. If present, it is in concentration less than 0.001 per-cent.

(2) Molybdenum interferes with detection of traces of copper. The latter, if present in this catalyst, is not present in concentration greater than about 0.001 per-cent.

(3) Vanadium interferes with detection of cadmium. The latter, if present in this catalyst, is not present in concentration greater than 0.001 per-cent, if it is present at all.

(4) Molybdenum interferes with detection of bismuth. The latter, is present in this catalyst, is not present in a concentration much greater than 0.01 per-cent.

(5) Standards were not available for making estimates of the silicon content of this catalyst. It appeared that this catalyst probably contained more than 1 per-cent of silicon, possibly somewhere in the range from 5 per-cent to 30 per-cent.

Table No. V

Experimental Data for Catalyst Number 2-R

Temperature degrees Centigrade	Time in hours	Pressure in millimeters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
200	1.00	50	109.0	57.64	2.19	++++	83.9	1.7	2.1	0.4	88.1	0.45	79.6
200	2.00	50	103.5	27.36	1.04	++++	79.6	2.4	3.0	0.3	82.8	0.36	94.2
200	3.00	50	100.7	17.75	0.67	++++	77.4	3.8	4.9	0.2	82.4	0.24	85.2
300	1.00	50	107.7	68.99	2.16	++++	82.7	4.4	5.3	0.8	84.2	0.95	88.4
300	2.00	50	105.2	33.69	1.06	++++	81.0	5.0	6.2	0.4	81.5	0.49	79.6
300	3.00	50	102.2	21.82	0.68	++++	78.6	5.4	6.9	0.2	78.6	0.25	84.0

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. + Indicates slight carbonization. + + Indicates noticable carbonization. + + + Indicates most of surface area carbonized. + + + + Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No. VI

Experimental Data for Catalyst Number **2-R**

Temperature degrees Centigrade	Time in hours	Pressure in milli- meters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
400	1.25	50	108.3	59.61	1.59	++++	83.4	3.5	4.2	4.0	85.5	4.6	88.0
400	2.50	50	105.7	29.09	0.78	++++	81.2	3.5	4.3	4.0	83.4	4.8	75.1
400	3.50	50	99.6	19.58	0.52	++++	76.7	4.8	6.3	5.0	77.0	6.5	72.9

1. Negative(-) indicates slight reduction.+? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization.+++Indicates most of surface area carbonized. + + ++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

CATALYST No. 2-R

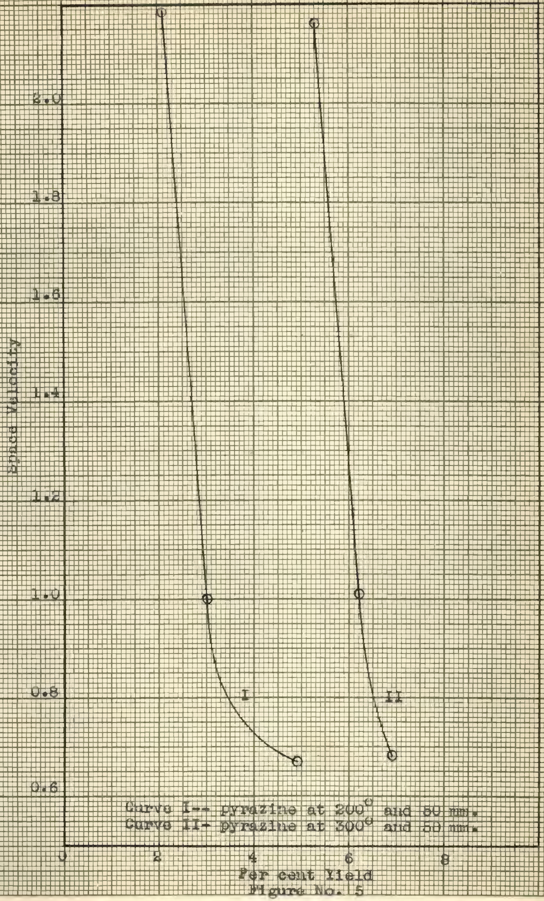


Figure No. 5

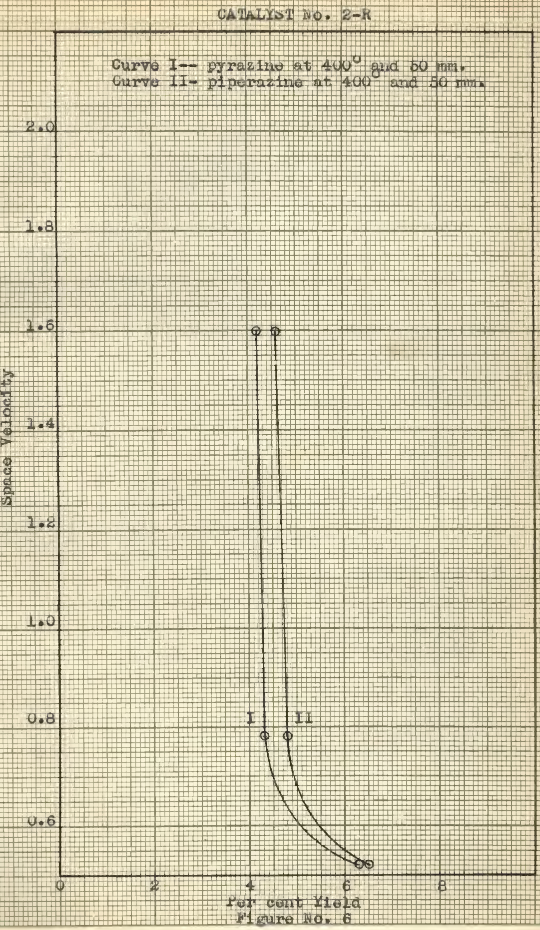

CATALYST No. 2-R
Curve I-- pyrazine at 400° and 50 mm.
Curve II- piperazine at 400° and 50 mm.
Space Velocity
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
I
II
0
2
4
6
8
Per cent Yield

Figure No. 6

3(e). GROUP THREE

Catalyst No. 3

Introduction

The catalyst used in these experiments was obtained from the Harshaw Chemical Company, Cleveland, Ohio. It is described as Mo-146, 1/8" tablets.

A spectrographic analysis was run on this catalyst. The interpretations of these analyses is subject to the same limitations for a spectrographic analysis as found in group one and two.

Observations

The main by-products found in the reacted mixture are: ethene diamine, ethyl aminoethanol, and acetaldehyde. Ethene diamine is found in every run in the pyrazine fraction which necessitated the extraction of the pyrazine fraction with ether to separate the pyrazine from the ethene diamine.

The catalyst was found to carbonize readily at temperatures from 200° to 400° at 50 mm. pressure. This condition necessitated that the catalyst be recalcined for 72.0 hours at 400° between each run.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 0.25: 1 at 200° and 50 mm.
ethene diamine: pyrazine:: 1.0 : 1 at 300° and 50 mm.
ethene diamine: pyrazine:: 1.2 : 1 at 400° and 50 mm.

The by-products were identified by the same derivatives as used in group one.

Spectrographic Analyses of Catalyst No. 3

Approximate lower limit of detection	Catalyst No. 3	Approximate lower limit of detection	Catalyst No. 3
Tl 0.1 %	______ %	Al 0.001 %	>>0.1 %
Sr 0.0005	______	Co 0.001	0.001
Li 0.001	(1)	Ni 0.001	0.001
Rb 0.05	______	Ag 0.0005	______
K 0.005	0.1	Cu 0.0005	(3)
Na ______	0.1	Cd 0.01	______
Ca ______	0.1	Ti 0.001	0.001
Mg ______	0.005	Mo 0.001	>> 0.1
Si ______	(2)	Be 0.001	______
Ba 0.0005	______	Bi 0.01	______
Fe 0.001	> 0.1	Sb 0.05	______
V 0.005	______	As 0.5	______
Y 0.01	______	Sn 0.001	______
Cr 0.001	0.005	Pb 0.001	______
Mn 0.001	______	Ge 0.001	______
W 0.1	______	In 0.001	______

Table No. VII

(1) Possible interference by molybdenum renders the identification of lithium uncertain in this catalyst. Lithium

appears to be present, but its concentration is certainly not in excess of 0.005 per-cent.

(2) Standards were not available for making estimates of the silicon content of this catalyst. It appeared that this catalyst probably contained more than 1.0 per-cent of silicon, although possibly somewhere in the range from 5.0 to 30.0 per-cent.

(3) Molybdenum interferes with detection of traces of copper. The latter, if present in this catalyst, is not present in concentration greater than about 0.001 per-cent.

Table No. **VIII**

Experimental Data for Catalyst Number 3.

Temperature degrees Centigrade	Time in hours	Pressure in milli- meters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
200	1.25	50	105.1	34.72	1.32	++	80.7	0.5	0.61	0.2	86.2	0.24	99.5
200	2.50	50	103.4	17.08	0.65	+++	79.4	0.8	1.00	0.2	84.5	0.23	98.0
200	4.00	50	99.8	10.30	0.39	++++	76.6	1.4	1.80	0.2	80.8	0.25	87.8
300	1.00	50	102.7	51.38	1.61	++++	78.8	2.0	2.50	1.8	82.6	2.20	85.1
300	2.50	50	98.1	19.63	0.62	++++	75.3	2.2	2.90	2.0	78.5	2.50	72.0
300	3.50	50	94.3	13.48	0.42	++++	72.4	2.4	3.30	2.0	75.2	2.70	79.9

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization. + + +Indicates most of surface area carbonized. + + ++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No. IX

Experimental Data for Catalyst Number 3

Grams of recovered N-(B-hydroxyethyl ethene diamine	Per cent yield of Piperazine[3]	Theoretical yield of Piperazine[3]	Grams of Piperazine obtained	Per cent Pyrazine obtained[2]	Grams of Pyrazine obtained	Theoretical yield of Pyrazine[2]	Condition of catalyst[1]	Space Velocity per hour at N.T.P.	Velocity of vapor reacted per hour	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Pressure in milli-meters	Time in hours	Temperature degrees Centigrade
57.0	4.60	70.5	3.2	5.90	4.1	69.6	++++	1.42	53.29	90.7	50	1.00	400
50.1	5.10	66.6	3.4	6.10	4.0	66.0	++++	0.60	22.43	85.9	50	2.25	400
41.5	5.70	63.7	3.6	6.80	4.3	63.6	++++	0.37	13.90	82.3	50	3.50	400

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization. + + +Indicates most of surface area carbonized. + + + +Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

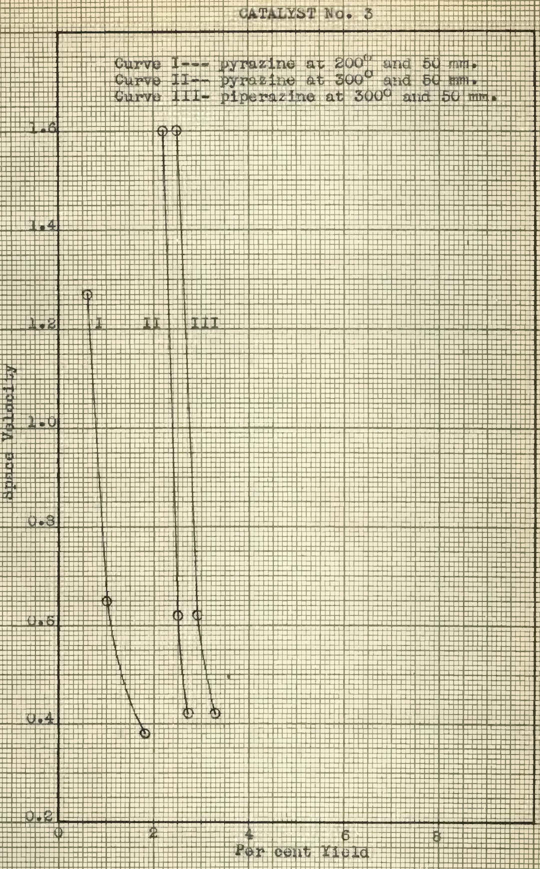
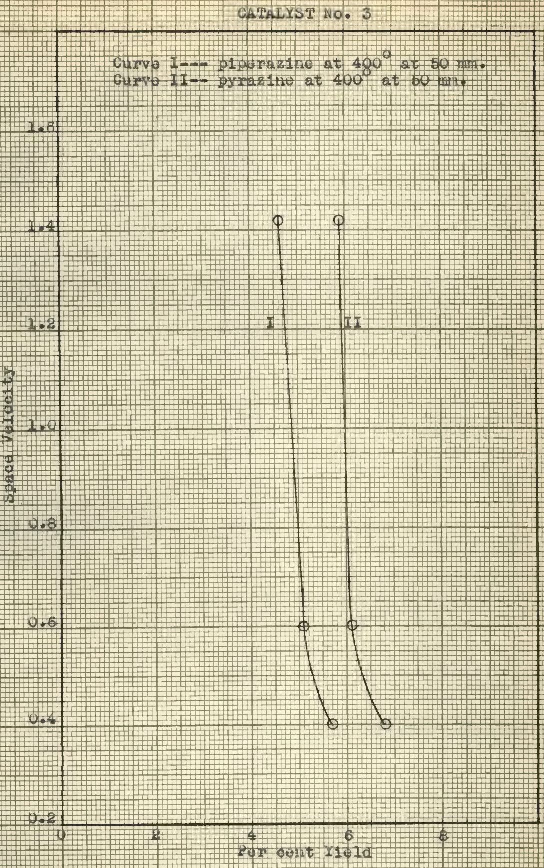

CATALYST No. 3
Curve I--- pyrazine at 200° and 50 mm.
Curve II-- pyrazine at 300° and 50 mm.
Curve III- piperazine at 300° and 50 mm.
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
I
II
III
Space Velocity
0
2
4
6
8
Per cent Yield

Figure No. 7



CATALYST No. 3

Figure No. 8

3(f). GROUP FOUR

Catalyst No. 4

Introduction

The catalyst used in these experiments was obtained from Wilkens-Anderson Company, Chicago, Ill. It is described as nickel pellet catalyst (U.O.P.). This catalyst is calcined, at the temperature at which it is to be used, with hot air. The catalyst was recalcined for 48 hours between each run. No spectrographic analysis was made on this catalyst.

Observations

Ethene diamine is found in each pyrazine fraction which necessitates an ether extraction to remove the pyrazine from the ethene diamine.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 1.2: 1 at 200° at 50 mm.
ethene diamine: pyrazine:: 1.4: 1 at 300° at 50 mm.
ethene diamine: pyrazine:: 1.6: 1 at 400° at 50 mm.

In the last two runs (No. 9 and 10), there was an excessive amount of non-condensable gases given off by the reaction. In both of these runs over half of the reacted material was lost as noncondensable material, due to decomposition of the starting material, N-(B-hydroxyethyl)ethene diamine.

When the tenth run was completed, the catalyst pellets were entirely broken down to black powder and the reaction tube was found to be stopped up with charcoal and powdered catalyst.

Other by-products obtained with this catalyst, are: ethyl aminoethanol, ethanol amine and traces of acetaldehyde. These products were identified by the same derivatives as used in group one.

Table No. X

Experimental Data for Catalyst Number 4.

Grams of recovered N-(B-hydroxyethyl ethene diamine	Per cent yield of Piperazine[3]	Theoretical yield of Piperazine[3]	Grams of Piperazine obtained	Per cent Pyrazine obtained[2]	Grams of Pyrazine obtained	Theoretical yield of Pyrazine[2]	Condition of catalyst[1]	Space Velocity per hour at N.T.P.	Velocity of vapor reacted per hour	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Pressure in millimeters	Time in hours	Temperature degrees Centigrade
92.8	0	86.0	0	1.20	1.0	81.0	++	0.87	22.96	105.5	50	1.25	200
92.7	0	87.1	0	1.30	1.1	82.1	++	0.49	12.92	106.9	50	2.25	200
93.8	0	82.8	0	1.70	1.3	78.3	+++	0.28	7.40	102.0	50	3.75	200
92.9	0	81.0	0	1.70	1.3	76.6	+++	0.26	6.78	99.8	50	4.00	200
98.8	1.10	87.9	1.0	3.10	2.6	84.4	+++	1.10	28.97	109.9	50	1.25	300
91.0	1.70	83.2	1.4	3.30	2.6	80.0	+++	0.52	13.73	104.2	50	2.50	300

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. + Indicates slight carbonization. + + Indicates noticable carbonization. ++ + Indicates most of surface area carbonized. + + ++ Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

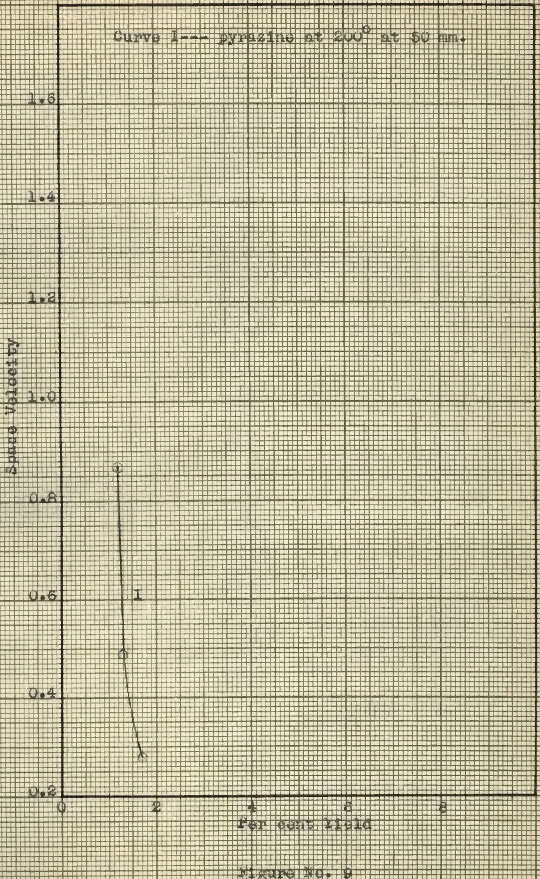
Table No. XI

Experimental Data for Catalyst Number 4.

Temperature degrees Centigrade	300	400	400	400		
Time in hours	4.00	1.25	2.25	4.00		
Pressure in millimeters	50	50	50	50		
Grams of reacted N-(B-hydroxyethyl) ethene diamine	104.7	95.6	115.2	118.9		
Velocity of vapor reacted per hour	8.63	29.60	19.82	11.50		
Space Velocity per hour at N.T.P.	0.33	1.12	0.75	0.31		
Condition of catalyst[1]	++++	++++	++++	++++		
Theoretical yield of Pyrazine[2]	80.4	73.4	88.5	91.3		
Grams of Pyrazine obtained	3.1	3.20	4.7	4.1		
Per cent Pyrazine obtained[2]	3.70	4.40	5.30	4.50		
Grams of Piperazine obtained	1.8	1.5	6.6	5.1		
Theoretical yield of Piperazine[3]	83.1	75.4	90.0	93.8		
Per cent yield of Piperazine[3]	2.20	2.00	7.30	5.40		
Grams of recovered N-(B-hydroxyethyl ethene diamine	92.3	70.3	44.5	35.0		

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization. + + +Indicates most of surface area carbonized. + + + +Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

CATALYST No. 4



Curve I--- pyrazine at 200° at 50 mm.

Figure No. 9

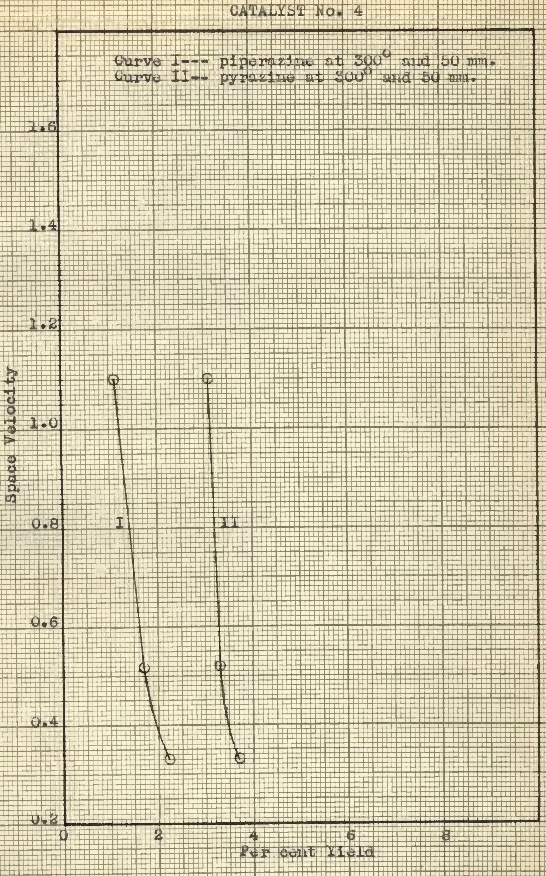

CATALYST No. 4
Curve I--- piperazine at 300° and 50 mm.
Curve II-- pyrazine at 300° and 50 mm.
Space Velocity
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
2
4
6
8
Per cent Yield
I
II

Figure No. 10

3(g). GROUP FIVE

Catalyst No. 5

Introduction

The catalyst used in these experiments is exploded vermiculite obtained from packing surrounding bromine bottles.

A spectrographic analysis was run on this catalyst. The interpretations of these analyses is subject to the same limitations for a spectrographic analysis as found in group one.

Observations

At 200° there is only slight charring of the catalyst whereas most of the surface is covered with carbon at 300°. When the charred catalyst is removed, from the reaction tube, several hours of blasting with a Bunsen burner is required to remove the carbon.

The catalyst was recalcined for 48 hours, at the temperature at which is was to be used, between each run.

Ethene diamine was found in every pyrazine fraction which necessitated the extraction of the pyrazine fraction with ether to separate the pyrazine from the ethene diamine.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 0.5: 1 at 200° and 50 mm.
ethene diamine: pyrazine:: 0.8: 1 at 300° and 50 mm.
ethene diamine: pyrazine:: 1.0: 1 at 400° and 50 mm.

Other by-products formed in the reaction are: acetaldehyde, ethyl aminoethanol, and ethanol amine. These by-products were identified by the same derivatives used in group one.

Spectrographic Analyses for Catalyst No. 5

Approximate lower limit of detection	Catalyst No. 5	Approximate lower limit of detection	Catalyst No. 5
Tl 0.1 %	______ %	Al 0.001 %	>0.10 %
Sr 0.0005	0.02	Co 0.001	0.01
Li 0.001	______	Ni 0.001	0.03
Rb 0.05	N.A.	Ag 0.0005	______
K 0.005	N.A.	Cu 0.0005	0.001
Na ______	N.A.	Cd 0.01	______
Ca ______	0.1	Ti 0.001	0.10
Mg ______	>>0.1	Mo 0.001	______
Si ______	>>0.1	Be 0.001	______
Ba 0.0005	0.03	Bi 0.01	______
Fe 0.001	>0.1	Sb 0.05	N.A.
V 0.005	0.03	As 0.50	______
Y 0.01	______	Sn 0.001	______
Cr 0.001	>0.1	Pb 0.001	______
Mn 0.001	0.1	Ge 0.001	______
W 0.10	______	In 0.001	0.01

Table No. XII

Table No. XIII

Experimental Data for Catalyst Number 5.

Temperature degrees Centigrade	Time in hours	Pressure in millimeters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
200	1.00	50	104.0	45.61	1.73	+	79.8	0.6	0.80	0.6	85.1	0.60	98.7
200	1.75	50	108.5	27.25	1.04	+	83.2	1.2	1.40	0.7	88.2	0.80	85.5
200	2.50	50	98.0	17.19	0.65	+	75.4	2.0	2.60	0.7	78.7	0.90	93.5
200	2.00	100	94.6	10.37	0.79	+++	73.9	1.2	1.60	0.7	76.7	0.90	89.5
200	6.00	400	90.0	0.46	0.14	+++	69.1	1.9	2.80	1.0	72.2	1.40	66.4
250	1.50	50	104.0	33.62	1.16	+	79.8	2.3	2.90	1.1	83.3	1.30	95.3

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. + Indicates slight carbonization. + + Indicates noticable carbonization. + + + Indicates most of surface area carbonized. + + + + Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No. XIV

Experimental Data for Catalyst Number 5.

Grams of recovered N-(B-hydroxyethyl ethene diamine	Per cent yield of Piperazine^3	Theoretical yield of Piperazine^3	Grams of Piperazine obtained	Per cent Pyrazine obtained^2	Grams of Pyrazine obtained	Theoretical yield of Pyrazine^2	Condition of catalyst^1	Space Velocity per hour at N.T.P.	Velocity of vapor reacted per hour	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Pressure in millimeters	Time in hours	Temperature degrees Centigrade
70.7	0.50	82.9	0.4	3.30	2.6	79.7	+	1.73	55.20	103.9	50	1.00	300
89.4	1.00	81.6	0.8	5.00	4.0	79.8	+	0.57	27.63	104.0	50	2.00	300
88.0	1.10	76.2	0.8	6.00	4.5	75.4	++	0.54	17.36	98.0	50	3.00	300
91.8	0.90	81.9	0.7	2.70	2.1	78.5	+++	0.85	13.55	102.0	100	2.00	300
79.5	0.90	76.4	0.7	2.50	1.8	72.9	+++	0.36	3.15	95.0	180	2.50	300
76.3	1.20	72.2	0.9	2.80	1.9	69.2	+++	0.34	1.34	90.0	400	2.50	300

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization. + + +Indicates most of surface area carbonized. + + + +Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No. XV

Experimental Data for Catalyst Number 5.

Temperature degrees Centigrade	Time in hours	Pressure in milli-meters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
400	1.25	50	107.0	53.42	1.43	+++	82.3	5.6	6.80	0.6	82.2	0.70	90.0
400	2.50	50	109.1	16.65	0.44	+++	83.8	8.1	9.70	0.8	81.3	1.00	90.5
400	3.75	50	107.6	10.95	0.29	+++	82.5	8.5	10.30	0.8	79.6	1.00	90.2

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization. + + +Indicates most of surface area carbonized. + + + +Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

CATALYST No. 5

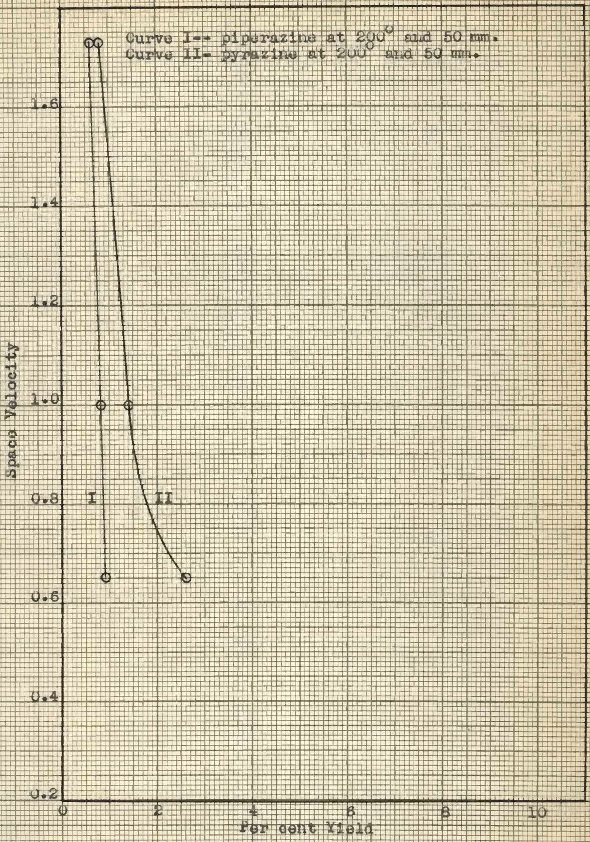


Figure No. 11

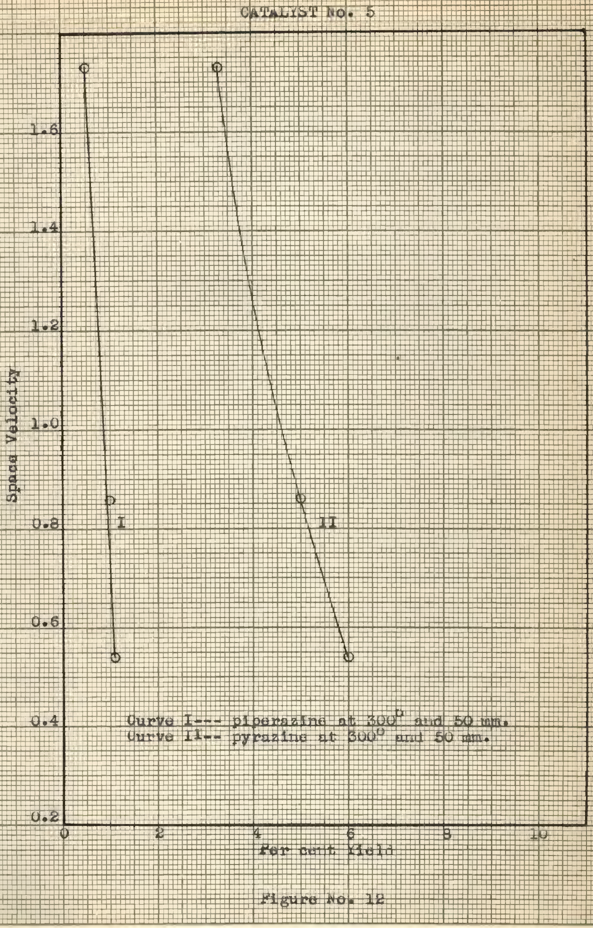

CATALYST No. 5
Space Velocity
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
2
4
6
8
10
Per cent Yield
I
II
Curve I--- piperazine at 300° and 50 mm.
Curve II-- pyrazine at 300° and 50 mm.

Figure No. 12

CATALYST No. 5

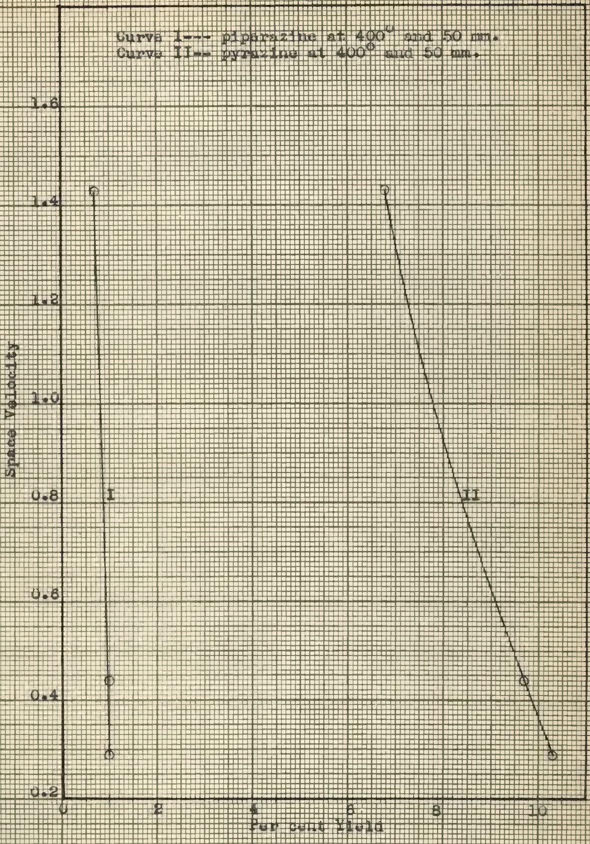


Figure No. 13

3(h). GROUP SIX

Catalyst No. 6

Introduction

The catalyst used in these experiments was obtained from the Davison Chemical Corporation, Baltimore, Maryland. It is described as 0.25 per-cent platinum on silica gel. The catalyst was calcined at the temperature at which it was to be used, with hot air in the reaction tube.

A spectrographic analysis was run on this catalyst. The interpretations of these analyses is subject to the same limitations for a spectrographic analysis as found in group one.

Observations

In the runs at 200° and 50 mm. pressure, very little ethene diamine was found in the pyrazine fraction. Very little acetaldehyde was found in the ternary benzene-ethanol-water azeotrope. The same products, ethene diamine and acetaldehyde were found in about the same proportion in the 300° runs at 50 mm. pressure. About twice as much ethene diamine was found in the runs at 400° and 50 mm. pressure. In the runs at 400° and 100 mm. pressure there were considerably larger amounts of ethene diamine found in the pyrazine fraction but the yield of acetaldehyde decreased as the pressure was increased.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 0.1: 1 at 200° and 50 mm.
ethene diamine: pyrazine:: 0.1: 1 at 300° and 50 mm.
ethene diamine: pyrazine:: 0.2: 1 at 400° and 50 mm.

Very small amounts of ethanol amine and ethyl aminoethanol were formed in the 400° runs at 50, 100 and 200 mm. pressure.

There was practically no charring in the reaction tube below 400°. At 400° there appeared noticeable amounts of carbon on the surface of the catalyst and on the reaction tube.

Spectrographic Analyses of Catalyst No. 6

	Approximate lower limit of detection	Catalyst No. 6		Approximate lower limit of detection	Catalyst No. 6
Tl	0.1 %	______ %	Al	0.001 %	0.002 %
Sr	0.0005	______	Co	0.001	______
Li	0.001	______	Ni	0.001	______
Rb	0.05	______	Ag	0.0005	______
K	0.005	______	Cu	0.0005	0.0005
Na	______	0.01	Cd	0.01	______
Ca	______	0.05	Ti	0.001	0.01
Mg	______	<0.005	Mo	0.001	______
Si	______	(1)	Be	0.001	______
Ba	0.0005	______	Bi	0.01	______
Fe	0.001	0.01	Sb	0.05	______
V	0.005	______	As	0.50	______
Y	0.01	______	Sn	0.001	______
Cr	0.001	______	Pb	0.001	______
Mn	0.001	______	Ge	0.001	______
W	0.1	______	In	0.001	______

Table No. XVI

(1) Standards were not available for making estimates of the silicon content of this catalyst. It appeared that this catalyst probably contains more than 1.0 per-cent of silicon, possibly somewhere in the range from 5.0 per-cent to 30.0 per-cent.

Table No. XVII

Experimental Data for Catalyst Number 6.

Temperature degrees Centigrade	Time in hours	Pressure in millimeters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
200	1.25	50	103.5	55.11	2.09	+?	79.6	0.2	0.25	0.2	85.2	0.23	93.8
200	2.50	50	102.6	27.32	1.04	+?	78.8	0.8	1.01	0.2	83.8	0.24	99.9
200	3.50	50	103.2	19.63	0.75	+?	79.3	1.0	1.26	0.3	84.1	0.36	98.3
300	1.25	50	104.0	52.80	1.66	+	79.8	2.6	3.30	3.2	83.0	3.90	96.5
300	2.25	50	101.8	28.71	0.90	+	78.0	3.3	4.20	4.0	80.5	5.00	89.0
300	3.75	50	103.0	17.43	0.55	+	79.0	4.4	5.60	6.3	80.3	7.90	84.2

1. Negative(-) indicates slight reduction.+? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization.+ + +Indicates most of surface area carbonized.+ + + +Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No. XVIII

Experimental Data for Catalyst Number 6.

Grams of recovered N-(B-hydroxyethyl ethene diamine	Per cent yield of Piperazine[3]	Theoretical yield of Piperazine[3]	Grams of Piperazine obtained	Per cent Pyrazine obtained[2]	Grams of Pyrazine obtained	Theoretical yield of Pyrazine[2]	Condition of catalyst[1]	Space Velocity per hour at N.T.P.	Velocity of vapor reacted per hour	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Pressure in milli-meters	Time in hours	Temperature degrees Centigrade
72.7	14.10	82.9	11.7	4.70	3.8	80.9	+	2.13	79.71	105.2	50	1.25	400
71.2	15.50	79.6	12.3	5.00	4.0	79.8	+	1.31	49.10	103.7	50	2.00	400
72.8	16.50	81.6	13.5	5.40	4.3	80.0	+	0.66	24.67	104.2	50	4.00	400
55.7	24.00	75.8	18.2	4.40	3.3	74.9	++	1.41	26.33	97.3	100	1.75	400
75.7	24.20	87.4	21.2	4.36	3.7	85.0	++	1.24	23.28	110.6	100	2.25	400
45.6	25.40	82.7	21.0	4.50	3.6	80.4	++	0.96	18.00	104.5	100	2.75	400

1. Negative(-) indicates slight reduction.+? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization.+++Indicates most of surface area carbonized.++++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No XIX

Experimental Data for Catalyst Number 6.

Temperature degrees Centigrade	Time in hours	Pressure in millimeters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
400	3.75	100	99.1	12.56	0.67	++	76.4	3.5	4.60	21.3	78.2	27.30	41.7
400	1.25	200	105.4	19.97	2.14	++	81.1	2.9	3.60	4.7	84.0	5.60	65.4
400	2.75	200	109.0	9.39	1.00	++	83.9	3.6	5.50	5.7	86.4	6.60	80.0
400	4.00	200	108.1	6.40	0.68	++	83.3	6.7	8.10	6.8	82.2	8.30	79.3
400	4.25	200	108.7	6.06	0.65	++	83.5	6.9	8.30	6.9	82.3	8.40	74.6

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization.+++Indicates most of surface area carbonized.++++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

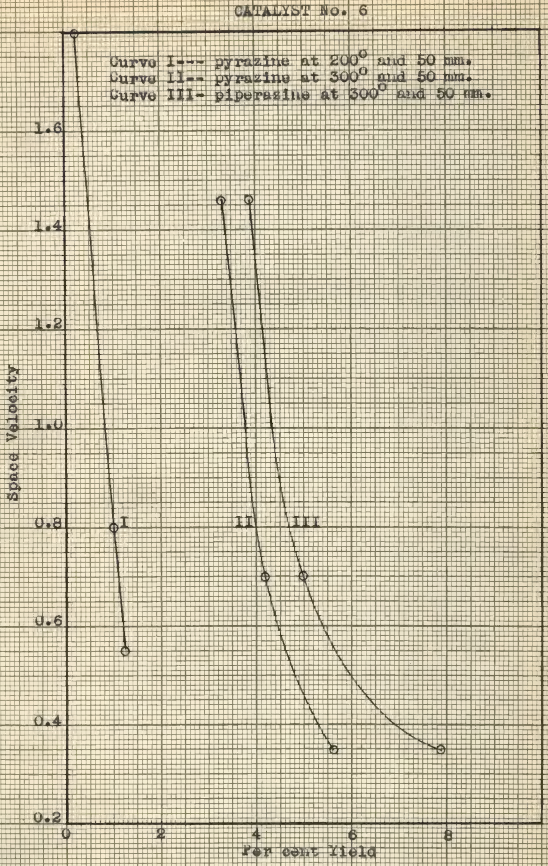

CATALYST No. 6
Curve I--- pyrazine at 200° and 50 mm.
Curve II-- pyrazine at 300° and 50 mm.
Curve III- piperazine at 300° and 50 mm.
Space Velocity
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
2
4
6
8
Per cent Yield
I
II
III

Figure No. 14

CATALYST No. 6

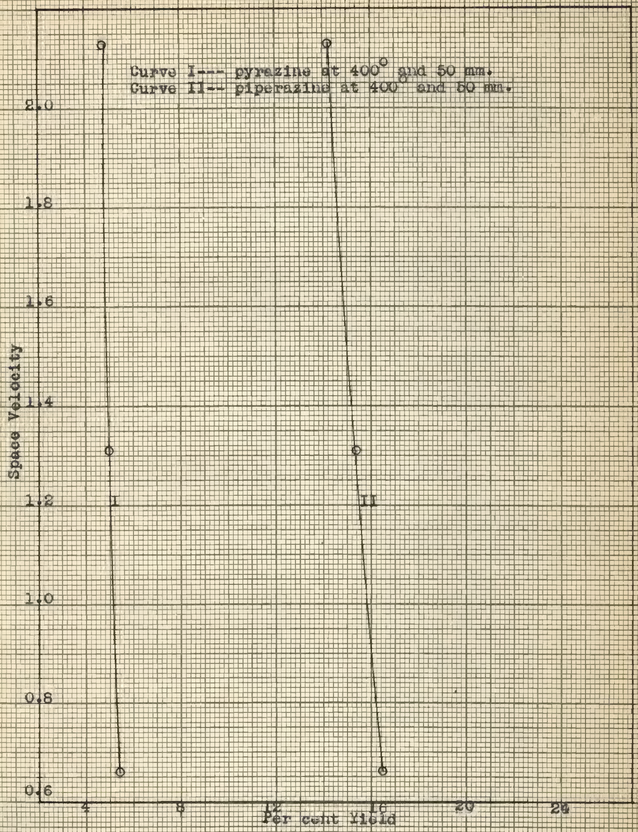


Figure No. 15

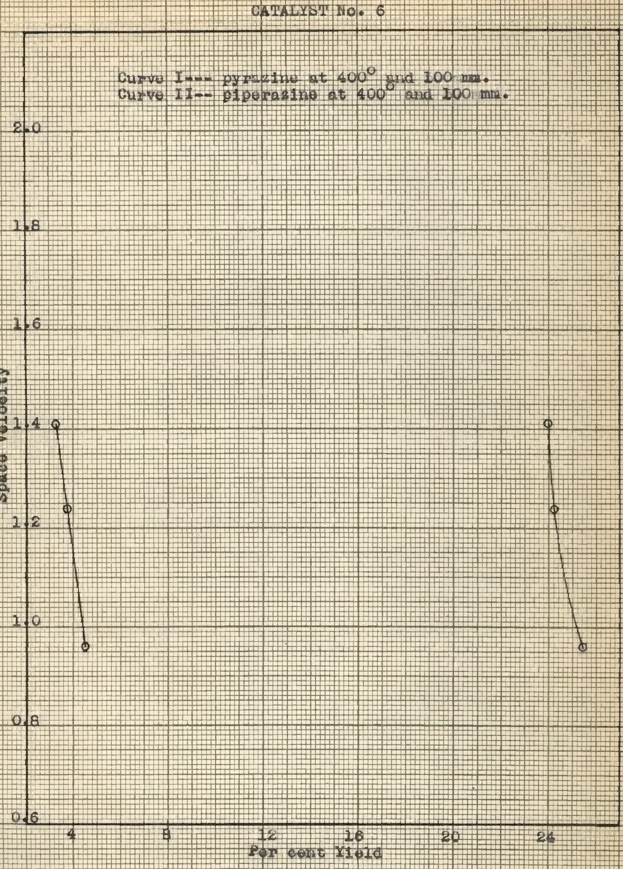

CATALYST No. 6
Curve I--- pyrazine at 400° and 100 mm.
Curve II-- piperazine at 400° and 100 mm.
2.0
1.8
1.6
1.4
1.2
1.0
0.8
0.6
Space Velocity
4
8
12
16
20
24
Per cent Yield

Figure No. 16

CATALYST No. 6

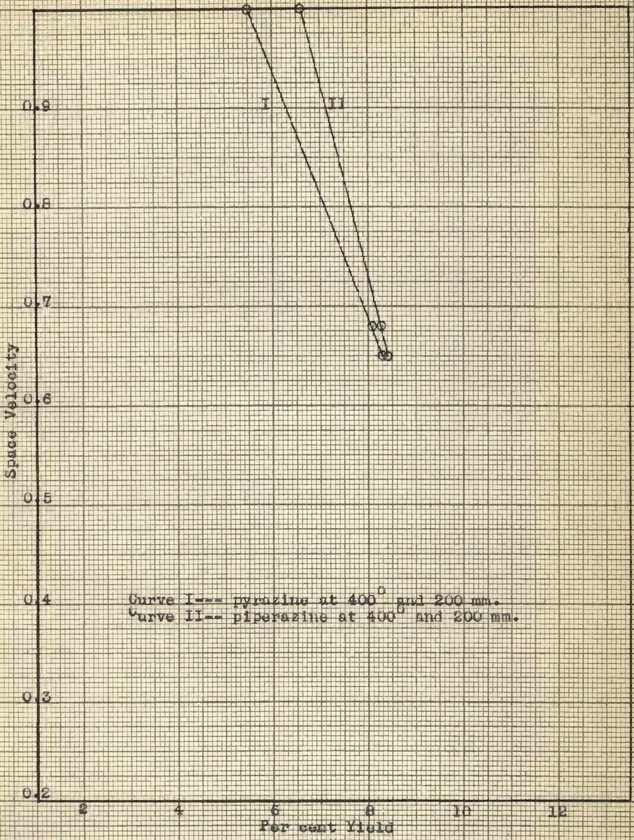


Figure No. 17

3(i). GROUP SEVEN

Catalyst No. 7

Introduction

The catalyst used in these experiments was obtained from the American Cyanamid and Chemical Corporation. This catalyst is described as vanadium catalyst which is used in contact sulfuric acid manufacture.

A spectrographic analysis was run on this catalyst. The interpretation of these analyses are subject to the same limitations for a spectrographic analysis, as found in group one.

Observations

At the beginning of each run, the catalyst appeared to be reduced and then a black film began to form on the catalyst.

Ethene diamine, ethanol amine, and ethyl aminoethanol are formed at 200°, 300° and 400° at 50 mm. pressure. The presence of ethene diamine in the pyrazine fraction necessitated the extraction of the pyrazine fraction with ether to remove the pyrazine from the ethene diamine.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 0.7: 1 at 200° and 50 mm.
ethene diamine: pyrazine:: 0.5: 1 at 300° and 50 mm.
ethene diamine: pyrazine:: 0.4: 1 at 400° and 50 mm.

Spectrographic Analyses of Catalyst No. 7

	Approximate lower limit of detection	Catalyst No. 7		Approximate lower limit of detection	Catalyst No. 7
Tl	0.1 %	— %	Al	0.001 %	0.1 %
Sr	0.0005	0.02	Co	0.001	0.002
Li	0.001	0.005	Ag	0.0005	—
Rb	0.05	—	Cu	0.0005	0.0005
K	0.005	>1.0	Cd	0.01	(2)
Na	—	1.0	Ti	0.001	0.02
Ca	—	0.5	Mo	0.001	—
Mg	—	0.1	Be	0.001	—
Si	—	(1)	Bi	0.01	—
Ba	0.0005	0.005	Sb	0.05	—
Fe	0.001	>0.1	As	0.5	—
V	0.005	>>0.1	Sn	0.001	—
Y	0.01	—	Pb	0.001	—
Cr	0.001	0.2	Ge	0.001	—
Mn	0.001	0.005	In	0.001	—
W	0.1	N.A.	Ni		—

Table No. XX

(1) Standards were not available for making estimates of the silicon content of this catalyst. It appeared that this catalyst probably contains more than 1.0 per-cent of silicon, possibly somewhere in the range from 5.0 per-cent to 30.0 per-

cent.

(2) Vanadium interferes with detection of cadmium. The latter, if present in this catalyst, is not present in concentration greater than about 0.05 per-cent.

Table No. XXI

Experimental Data for Catalyst Number 7.

Grams of recovered N-(B-hydroxyethyl ethene diamine	Per cent yield of Piperazine[3]	Theoretical yield of Piperazine[3]	Grams of Piperazine obtained	Per cent Pyrazine obtained[2]	Grams of Pyrazine obtained	Theoretical yield of Pyrazine[2]	Condition of catalyst[1]	Space Velocity per hour at N.T.P.	Velocity of vapor reacted per hour	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Pressure in milli-meters	Time in hours	Temperature degrees Centigrade
88.5	0.20	84.6	0.2	1.90	1.5	80.4	+++	1.10	28.50	104.5	50	1.25	200
101.0	0.20	85.4	0.2	2.10	1.7	81.3	++++	0.70	18.00	105.7	50	2.00	200
94.0	0.300	84.7	0.3	2.50	2.0	81.0	++++	0.30	8.40	105.2	50	4.25	200
102.6	0.30	89.1	0.3	2.00	1.7	84.7	++++	0.90	30.30	110.1	50	1.50	300
83.1	0.30	71.2	0.2	2.60	1.8	68.2	++++	0.60	18.30	88.6	50	2.00	300
93.7	0.50	82.2	0.4	2.80	2.2	78.7	++++	0.40	12.10	102.5	50	3.50	300

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. + Indicates slight carbonization. + + Indicates noticable carbonization. + + + Indicates most of surface area carbonized. + + + + Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No. XXII

Experimental Data for Catalyst Number 7.

Temperature degrees Centigrade	400	400	400			
Time in hours	1.25	2.25	4.00			
Pressure in millimeters	50	50	50			
Grams of reacted N-(B-hydroxyethyl) ethene diamine	111.4	104.6	106.3			
Velocity of vapor reacted per hour	43.30	22.50	12.90			
Space Velocity per hour at N.T.P.	1.20	0.60	0.30			
Condition of catalyst[1]	++++	++++	++++			
Theoretical yield of Pyrazine[2]	85.7	80.4	81.9			
Grams of Pyrazine obtained	1.4	1.3	1.5			
Per cent Pyrazine obtained[2]	1.60	1.70	1.80			
Grams of Piperazine obtained	6.3	6.3	0.5			
Theoretical yield of Piperazine[3]	90.5	84.9	86.1			
Per cent yield of Piperazine[3]	0.30	0.30	0.60			
Grams of recovered N-(B-hydroxyethyl ethene diamine	92.5	92.0	90.0			

1. Negative(-) indicates slight reduction. +? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization. + + +Indicates most of surface area carbonized. + + + +Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

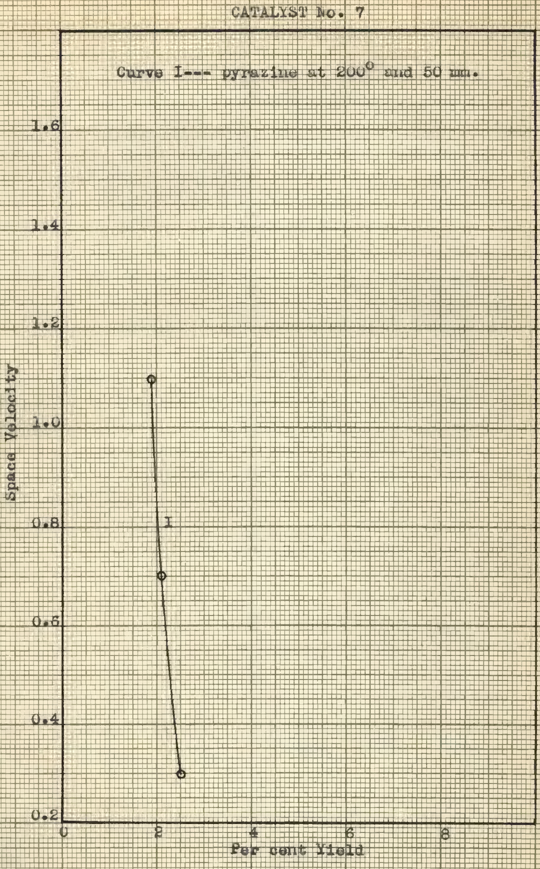

CATALYST No. 7
Curve I--- pyrazine at 200° and 50 mm.
Space Velocity
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
I
0
2
4
6
8
Per cent Yield

Figure No. 18

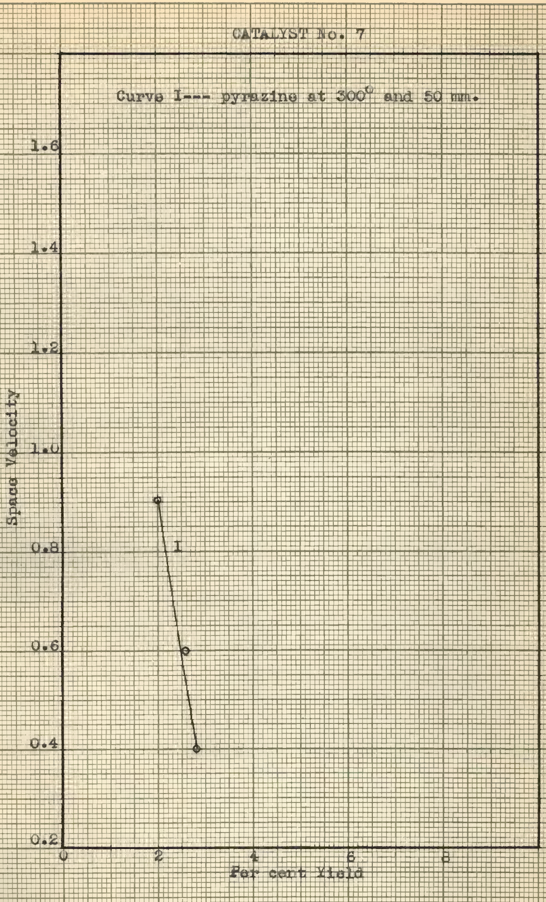

CATALYST No. 7
Curve I--- pyrazine at 300° and 50 mm.
Space Velocity
1.6
1.4
1.2
1.0
0.8
0.6
0.4
0.2
0
2
4
6
8
Per cent Yield
I

Figure No. 19

CATALYST No. 7

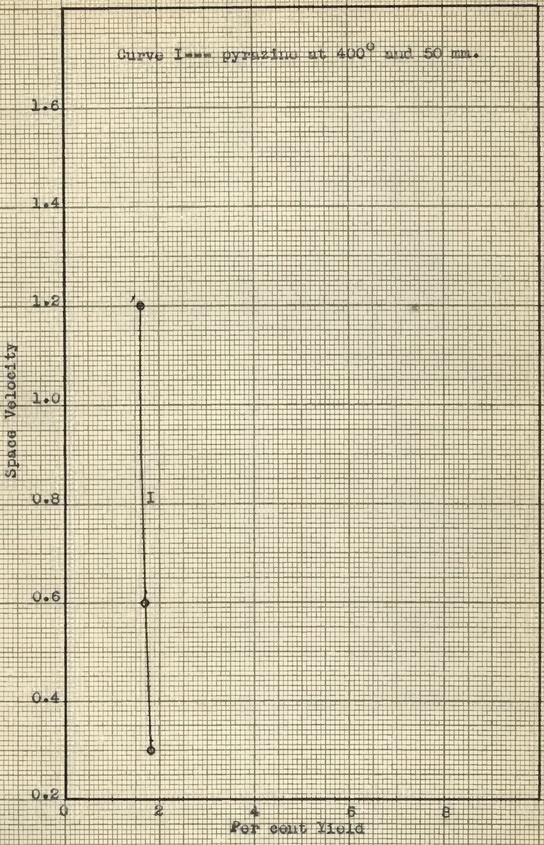


Figure No. 20

3(j). GROUP EIGHT

Catalyst No. 8

Introduction

The catalyst used in these experiments was obtained from the Will Corporation, Rochester, New York. It is described as 5.0 per-cent platinized asbestos.

This catalyst was calcined with hot air, at the temperature at which it was to be used, for 48 hours. The catalyst was recalcined for 48 hours between each run.

High space velocities with this catalyst, as compared with other catalysts used, are due to the small volume of catalyst used in these experiments. No spectrographic analyses were run on this catalyst.

Observations

The charring of this catalyst is doubtful at 200° and 50 mm. whereas at 300° and 400° at 50 mm. the charring is noticeable.

Ethene diamine was found in every pyrazine fraction which necessitated the extraction of the pyrazine fraction with ether to remove the pyrazine from the ethene diamine.

Ratio of ethene diamine to pyrazine;

ethene diamine: pyrazine:: 1.9: 1 at 200° and 50 mm.
ethene diamine: pyrazine:: 1.4: 1 at 300° and 50 mm.
ethene diamine: pyrazine:: 1.2: 1 at 400° and 50 mm.

A fraction boiling at 162° to 165° was found in each run. The quantity of material in this fraction increased with the temperature of the experiment. This material was found to consist of N-(B-hydroxyethyl)ethene diamine, piperazine and an aldehyde of unknown identity. The 2, 4-dinitrophenylhydrazone derivative of the aldehyde has a melting point of 108° to 109°. This aldehyde was not isolated in pure form.

Other by-products found in these experiments are: ethanol amine and ethyl aminoethanol which were identified by the same derivatives as in group one.

Table No. XXIII

Experimental Data for Catalyst Number 8.

Temperature degrees Centigrade	Time in hours	Pressure in millimeters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
200	1.25	50	109.7	165.5	6.30	+?	84.2	1.3	1.50	0.2	89.1	0.20	106.6
200	2.75	50	100.7	69.1	2.60	+?	77.3	1.3	1.70	0.2	81.7	0.20	92.4
200	4.00	50	107.2	50.5	1.90	+?	82.3	1.6	1.90	0.2	86.7	0.20	100.9
300	1.25	50	114.5	209.3	6.60	+	87.9	2.1	2.40	0.2	92.2	0.20	108.6
300	2.25	50	111.1	112.8	3.50	+	85.2	2.2	2.70	0.4	89.3	0.40	99.7
300	3.75	50	110.0	67.0	2.10	+	84.5	2.6	3.10	0.3	88.0	0.30	100.6

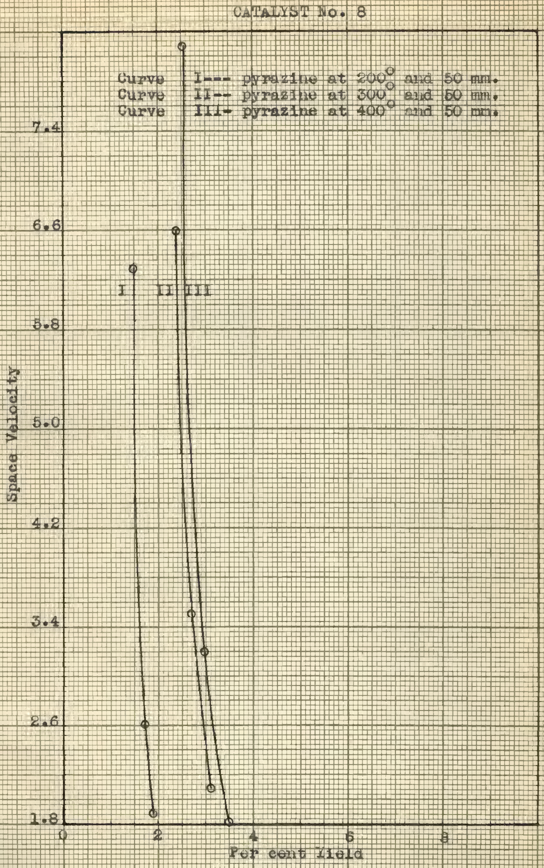
1. Negative(-) indicates slight reduction.+? Indicates doubtful carbonization. +Indicates slight carbonization. ++Indicates noticable carbonization.+++Indicates most of surface area carbonized.++++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.

Table No. XXIV

Experimental Data for Catalyst Number 8.

Temperature degrees Centigrade	Time in hours	Pressure in milli-meters	Grams of reacted N-(B-hydroxyethyl) ethene diamine	Velocity of vapor reacted per hour	Space Velocity per hour at N.T.P.	Condition of catalyst[1]	Theoretical yield of Pyrazine[2]	Grams of Pyrazine obtained	Per cent Pyrazine obtained[2]	Grams of Piperazine obtained	Theoretical yield of Piperazine[3]	Per cent yield of Piperazine[3]	Grams of recovered N-(B-hydroxyethyl ethene diamine
400	1.00	50	112.8	302.7	8.20	+++	86.6	2.5	2.90	0.2	90.3	0.20	101.5
400	2.50	50	112.7	120.9	3.20	+++	86.5	2.7	3.10	0.3	90.8	0.30	96.6
400	4.50	50	110.8	66.1	1.80	+++	85.1	3.0	3.50	0.3	88.2	0.30	88.2

1. Negative(-) indicates slight reduction.+? Indicates doubtful carbonization. +Indicates slight carbonization. + +Indicates noticable carbonization.+++Indicates most of surface area carbonized.++++Indicates surface totally carbonized.
2. Based on total number of grams of N-(B-hydroxyethyl)ethene diamine.
3. See example of calculations on page 72.



CATALYST No. 8

Figure No. 21

4. SUMMARY OF EXPERIMENTAL

Berkman (21a) points out the fact that when per-cent yield is plotted against the reciprocal of Space Velocity, the equilibrium is shifted to the right with increased temperature. It was found that dehydrogenation was accelerated at the same contact time by either an increase in temperature or a decrease in pressure. This was found to be generally true in the present investigation. Ipatieff (116a), however, disagrees with the data of Berkman in his dehydrogenation experiments and quotes the conclusions of Palmer and Constable as follows: "The velocity of hydrogen liberation depends neither upon the velocity at which the substance is passed through the catalyst nor upon the pressure".

The experimental work carried out in these investigations involves the simultaneous dehydrogenation of N-(B-hydroxyethyl)ethene diamine. It was found in most cases that, as the temperature is increased, the dehydration reaction is more predominant with only slight increase in the dehydrogenation reaction.

In several cases, the yield of the dehydrogenation reaction was found to be less at higher temperatures than it was at lower temperatures. Where this condition existed, there was always noticeable carbon formation on the catalyst. Berkman (21a) shows that, in the dehydrogenation of olefins, carbon formation is considerably higher than in the dehydrogenation of paraffins. It is pointed out by Berkman that the carbon formation is favored by keeping the reaction products too long in contact with the catalyst, and conversely, can be minimized by operating at higher Space Velocities. The reason for decreased yields of the dehydrogenation products in this investigation appears to be due largely to the fact that some of the partially dehydrogenated reaction products may be in contact with the catalyst for too long a time.

In the series of investigations using catalyst No. 1., it was found that there was a slight increase of the dehydrogenation product, pyrazine, and practically none of the dehydration product, piperazine, when the temperature was increased from 200° to 300°. However, when the temperature was raised to 400°, the dehydrogenation product, pyrazine, decreased and a noticeable increase of piperazine appeared. The yield of dehydrogenated product dropped back to approximately the yields obtained at 200° when the reaction was carried out at 400° and 50 mm. pressure. The results of this series of experiments are clearly shown in Tables II and III.

Catalyst No. 2-R is unsatisfactory for general use because of excessive carbon formation on the catalyst. The yield of the dehydrogenation product, pyrazine, at 200° was as good as with catalyst No. 1., whereas the yield of pyrazine at 300° was approximately a third greater than was found with catalyst No. 1. The yields of the dehydration product, piperazine, were in slightly larger amounts than was found with catalyst No. 1. The yields of piperazine, however, were so small that an increase in temperature from 200° to 300° produced a negligible effect. With this catalyst, the same phenomena appeared as with catalyst No. 1. When the reaction tube was operated at 400° the yields of pyrazine dropped below those found at 300° and the yields of piperazine materially increased to slightly greater than the yields of pyrazine. In this case the yield of piperazine was less than those found for catalyst No. 1 at the same Space Velocities. In general, catalyst No. 2-R is inferior to catalyst No. 1, because of lower yields of the desired products, pyrazine and piperazine and the presence of excessive amounts of carbon on the catalytic surfaces.

In the series of experiments carried out with catalyst No. 3., the curves obtained by plotting Space Velocity against per-cent yield did not show a consistency of shape as was found with curves obtained in the experiments with catalyst No. 1 and catalyst No. 2-R. The curve obtained with catalyst No. 3 at 200° and 50 mm. pressure showed a rapid increase in yield of the dehydrogenation product, pyrazine, with decreasing Space Velocity. There was very little dehydration product, piperazine, formed at 200°. When the temperature was increased to 300°, a very marked increase of carbon was deposited on the catalytic surface. The shape of the curve at 300° showed a close resemblance to the curves of catalyst No. 1 and No. 2-R at 300°. The yields of both pyrazine and piperazine were less than the yields obtained with catalysts No. 1 and No. 2-R at 200° and 300°. However, at 400° the yields of pyrazine and piperazine with catalyst No. 3 approached the yields obtained with catalyst No.1 and No. 2-R. Catalyst No. 3 and catalyst No. 2-R are both considered inferior to catalyst No. 1 from the standpoint of yields of pyrazine and piperazine. Catalyst No. 4 gave higher yields of pyrazine at higher Space Velocities than catalyst No. 3 but much less than the yields obtained with catalyst No. 1 and No. 2-R at corresponding Space Velocities at 200°. The yields of pyrazine at 300° and 400° were far below the yields of pyrazine obtained with catalyst No. 1, No. 2-R, and No. 3, at the corresponding temperatures and Space Velocities.

In the experiments with catalyst No. 4 at 300°, the yields of piperazine were below the yields of pyrazine whereas at 400° the yields of piperazine appeared to be higher than the yields of pyrazine. There was a large volume of non-condensable gases at a Space Velocity of 0.31 at 400° and the yields of pyrazine and piperazine were reduced below the yields of pyrazine and piperazine obtained at a Space Velocity of 0.75 and 400°. The reduced yield was probably due to the fact that the reaction products were in contact with the catalyst for too long a period of time which led to excessive decomposition.

Catalyst No. 5 is superior to catalysts No. 3 and No. 4 and inferior to catalysts No. 1 and No. 2-R from the standpoint of yields of pyrazine at similar Space Velocities and temperatures. When the temperature was increased, the curve represented by Space Velocity vs. per cent yield was shifted to the right as predicted by Berkman (21a). The dehydrogenation product, pyrazine, was the main reaction product derived from these experiments. The dehydration product, piperazine, was always found in very small amounts. The largest yield of piperazine, 1.4 per-cent, was obtained at a Space Velocity of 0.14.

A series of experiments was carried out with catalyst No. 6. This catalyst was found to be superior to all of the other catalysts used in these series of investigations. The prediction of Berkman, that the curve would shift to the right on increased temperature, was found to hold up to 400° and 100 mm. pressure. At 200° and 50 mm. pressure, the yields of the hydrogenation product, pyrazine, were lower than found with the other catalysts, namely numbers 1, 2-R, 3, 4, and 5. The yields of the dehydrogenation product, piperazine, were practically negligible at 200° and 50 mm. pressure. At 300° and 50 mm. pressure, the yields of pyrazine were approximately four times greater than those obtained at 200° and 50 mm. pressure and the yields of piperazine were slightly greater than the yields of pyrazine.

This shows that as the temperature is increased and the pressure held constant, the dehydration reaction predominates over the dehydrogenation reaction. When the experiments were carried out at 400° and 50 mm. pressure, the yields of the dehydrogenation product, pyrazine, increased very little; whereas the yields of the dehydration product, piperazine, increased approximately three times as much as was found at 300° and 50 mm. pressure. There was very little carbon deposited on the catalytic surfaces during the runs at 400° and 50 mm. pressure. The series of experiments carried out at 50 mm. pressure confirmed the predictions of Berkman that dehydrogenation is increased with increased temperature.

In order to get further evidence, the temperature was maintained at 400° and the pressure was increased. At 400° and 100 mm. pressure, the yields of pyrazine were decreased and the yields of piperazine were slowly increased with very little evidence of charring. The increase in pressure to 100 mm. caused a slight change in the shape of the curve, a slight reduction in yields of the dehydrogenation product, and an increase in yields of the dehydration product. When the temperature was maintained at 400° and the pressure changed to 200 mm., the shape of the curve was changed again and there was a noticeable decrease in the dehydration yields that closely approached the yields of the dehydrogenation product.

A series of experiments was run on catalyst No. 7 at 50 mm. pressure. In all of these experiments the per-cent yield of the dehydration product, piperazine, was negligible. This catalyst is inferior to catalysts No. 1, No. 2-R, No. 3, No. 4, No. 5, and No. 6. The yields of pyrazine increased slightly when the temperature was increased from 100° to 200° at 50 mm. pressure. When the temperature was increased to 400° at 50 mm. the yields of pyrazine decreased below the yields obtained at 200° and 300°. There was an excessive amount of carbon deposited on the catalytic surfaces at 400°. The reason for this decrease in yields of pyrazine could be explained by the prolonged contact between the reaction products and the catalyst.

In the series of experiments investigated with catalyst No. 8, it was found that the per-cent yields of pyrazine were below the per-cent yields obtained with the other catalysts investigated. With this catalyst, there appeared to be more molecular fission and side reactions than occurred with the other seven catalysts. This catalyst is definitely inferior as a catalyst for ring formation by dehydration of N-(B-hydroxyethyl)ethene diamine and subsequent dehydrogenation of the ring compound.

5. CONCLUSION

Apparatus was designed and constructed which permitted positive control of vapor velocities and heating of the catalyst for vapor-phase reaction studies at normal and reduced pressures.

Eight catalysts were studied to determine the per-cent yields of two heterocyclic ring compounds that could be obtained with these catalysts.

It was found that catalyst No. 6 was the best catalyst for the ring closure of N-(B-hydroxyethyl)ethene diamine to give piperazine and simultaneous dehydrogenation of piperazine to give pyrazine. A yield of 28 per-cent piperazine and 8 per-cent pyrazine was obtained with this catalyst.

The highest yield of pyrazine, 10 per-cent, was obtained with catalyst No. 5.

Three control runs were made in the apparatus without a catalyst. A run at 200° and 50 mm. pressure at a Space Velocity of 0.14 was made and no pyrazine or piperazine was obtained. Similarly runs were made at 300° and 400° at 50 mm. pressure at Space Velocity of 0.2 and 0.25 respectively. No pyrazine or piperazine was obtained in these experimental runs.

BIBLIOGRAPHY

1. Abderhalden, Klarmann, Schwab: Z. physiol. Chem., 135 180-7, (1924); Chem. Abstr., 18, 2901, (1924)

2. Abderhalden, Komm: Z. physiol. Chem., 139, 181, (1924); Z. physiol. Chem., 140, 99-108, (1924); Chem. Abstr., 19, 995, (1925)

3. Abenius: J. prakt. Chem., (2) 40, 425; J. Chem. Soc., 58, 268, (1890)

4. Abenius: J. prakt. Chem., (2) 41, 79, (1890); J. Chem. Soc., 58, 525, (1890)

5. Abenius; J. prakt. Chem., (2) 47, 183, (1893); J. Chem. Soc. Abstr., i, 1893, 374, (1893)

6. Adkins: "Reactions of Hydrogen", Univ. of Wisconsin Press, Madison (1937), page 13

6a. Adkins, Cramer: (a) J. Am. Chem. Soc., 52, 4354, (1930); Chem. Abstr., 25, 89, (1931)
(b) U. S. Patent 2, 058, 547 (Oct. 27, 1936); Chem. Abstr., 31, 110, (1937)

7. Amendsen: J. Chem. Education, 16, 566, (1939); Chem. Abstr., 31, 3451, (1937)

8. Amendsen: Rept. New Engl. Assoc. Chem. Teachers, 41, 73, (1939); Chem. Abstr., 34, 1522, (1940)

9. Abderhalden, Schwab: Z. physiol. Chem., 149, 100, (1925); Chem. Abstr., 20, 57, (1926)

10. Aspinall: J. Am. Chem. Soc., 62, 1202, (1940); Chem. Abstr., 34, 6285, (1940)

11. Aston: J. Am. Chem. Soc., 52, 4172, (1930); Chem. Abstr., 24, 5755, (1930); Chem. Abstr., 24, 3792, (1930)

12. Aston: J. Am. Chem. Soc., 52, 5254, (1930); Chem. Abstr., 25, 516, (1931)

13. Aston, Peterson, Holowchak: J. Am. Chem. Soc., 56, 153, (1934); Chem. Abstr., 28, 1703, (1934)

14. Aston, Ailman, Schenermann, Koch: J. Am. Chem. Soc., 56, 1163, (1934); Chem. Abstr., 28, 4423, (1934); Chem. Abstr., 28, 1702, (1934)

15. Avy: Bull. soc. chim. (4) 49, 514, (1931); Chem. Abstr., 25, 4271, (1931)

16. Bain: Dissertation, University of Florida (1939)

17. Bain, Pollard: J. Am. Chem. Soc., 61, 532, (1939); Chem. Abstr., 33, 3138, (1939)

18. Bain, Pollard; J. Am. Chem. Soc., 61, 2704, (1939)

19. Bayer & Co: German Patent 74, 628; Friedlander's Fortschritte der Theerfarbenfabrication III, 957 (Springer, Berlin)

20. Bean, Spies: Am. Heart J., 20, 62, (1940); Chem. Abstr., 34, 7442, (1940)

21. Beilsrein's Handbook der Organischen Chemie, 4th edit., Vol. 23, page 93, (1936)

21a. Berkman, Marrell, Egloff: "Catalysis", Reinhold Pub. Co., (1940)

22. Biedbach, Weigand: Arch. Pharm., 279, 101, (1941); Chem. Abstr., 35, 6059, (1941)

23. Billman, Rendall: J. Am. Chem. Soc., 66, 540, (1944); Chem. Abstr., 38, 2651, (1944)

24. Bills, McDonald, Spies: Southern Med. J. 32, 793, (1939); Chem. Abstr., 33, 7853, (1939)

25. Birkofer: Ber., 75B, 429, (1942); Chem. Abstr., 37, 3067, (1943)

26. Bischler: Ber., 24, 717, (1891); J. Chem. Soc. Abstr., 60, 735, (1891)

27. Bodshow, Stephen, Weizmann: J. Chem. Soc., 107, 803, (1915); Chem. Abstr., 9, 2517, (1915)

28. Bradley, Robinson: J. Chem. Soc., 1932, 1254, (1932)

29. Brandes, Stoehr: J. prakt. Chem., (2) 54, 481, (1896); J. Chem. Soc., 1897, i, 230, (1897)

30. Brgstrom, Ogg: J. Am. Chem. Soc., 53, 245, (1931); Chem. Abstr., 24, 4038, (1930); Chem. Abstr., 25, 957, (1931)

31. Britton, Nutting, Petrie: U. S. Patent 2, 164, 564, (July 4, 1939); Chem. Abstr., 33, 8167, (1939)

32. Brown, Reid: J. Am. Chem. Soc., 46, 1836, (1924): Chem. Abstr., 18, 2875, (1924)

33. Bruhl: Z. physiol. Chem. 22, 373, (1897); J. Chem. Soc. Abstr., 1897, ii, 297, (1897)

34. Brusen: U. S. Patent 2,229,024, (Jan. 21, 1941); Chem. Abstr., 35, 3009, (1941)

35. Bucherer, Seyde: J. prakt. Chem., (2) 75 264

36. Buchman, Reims, Skei, Sehlatter: J. Am. Chem. Soc., 64, 2696, (1942); Chem. Abstr., 37, 613, (1943); Chem. Abstr., 37, 2701, (1943)

37. Butlcher: Ber., 46, 3084, (1913); Chem. Abstr., 8, 126, (1914); Chem. Abstr., 2, 851, (1908)

38. Callomon, Linton: J. Lab. Clin. Med., 29, 574, (1944); Chem. Abstr., 38, 5971, (1944)

39. Campbell, Haworth, Perkin: J. Chem. Soc., 129, 32, (1926); Chem. Abstr., 19, 2958, (1925); Chem. Abstr., 20, 1083, (1926)

40. Carbide and Carbon Chemical Corp: French Patent 823, 471, (Jan. 20, 1938); Chem. Abstr., 32, 5414, (1938)

41. Carbide and Carbon Chemical Corp.: (A.L.Wilson, inventor) German Patent 678, 154 (July 11, 1939)

42. Carbide and Carbon: "Technical Papers", 1938

43. Chattaway, Humphry: J. Chem. Soc., 1929, 645, (1929); Chem. Abstr., 23, 3473, (1929)

45. Chem. Fabrik. Schering: Ger. Pat. 60, 547; Frdl.[1], III, 948

46. Chem. Fabrik. Schering: Ger. Pat. 63, 618; Frdl.[1], III, 949

47. Chem. Fabrik. Schering: Ger. Pat. 65,236

48. Chem. Fabrik. Schering: Ger. Pat. 65, 347; Frdl.[1], III, 949

49. Chem. Fabrik. Schering: Ger. Pat. 66,461; Frdl.[1], III, 951

50. Chem. Fabrik. Schering: Ger. Pat. 67, 811; Frdl.[1], III, 954

51. Chem. Fabrik. Schering: Ger. Pat. 70, 056; Frdl.[1], III, 953

52. Chem. Fabrik. Schering: Ger. Pat. 71, 576; Frdl.[1], III, 950

53. Chem. Fabrik. Schering: Ger. Pat. 73, 125; Frdl.[1], III, 953

54. Chem. Fabrik. Schering: Ger. Pat. 73, 354; Frdl.[1], III, 965

55. Chem. Fabrik. Schering: Ger. Pat. 77, 351; Frdl.[1], III, 1202

56. Chem. Fabrik. Schering: Ger. Pat. 79, 121; Frdl.[1], IV, 1203

57. Chem. Fabrik. Schering: Ger. Pat. 83, 524; Frdl.[1], IV, 1203

58. Chem. Fabrik. Schering: Ger. Pat. 98, 031; Chem. Zentr., 1898, ii, 743, (1898)

59. Chem. Fabrik. Schering: Ger. Pat. 100,232; Chem. Zentr., 1899, i, 719, (1899)

60. Chem. Fabrik. Tempelhof A.-G. (Josef Zeltner, inventor): Ger. Pat. 591, 808 (Jan. 27, 1934); Chem. Abstr., 28, 2849, (1934)

[1] Frdl.: Friedlander's Fortschritte der Theerfarbenfabrication, Springer, Berlin; cf. Beilstein's "Handbook of Organic Chemistry", Springer, Berlin, (IV) 23, 4

61. Chichibobin, Schubina: J. Russ. Phys.-Chem. soc., 62, 1189, (1930); Chem. Abstr., 25, 2728, (1931)

62. Chichibobin, Shchukina: Ber., 62B, 1075, (1929); Chem. Abstr., 23, 4218, (1929)

63. Chitwood, McNamee: U. S. Patent 2,345,237 (March 28, 1944) assigned to Carbide and Carbon

64. Chitwood: U. S. Patent 2, 345, 236 (March 28, 1944) assigned to Carbide and Carbon

65. Colesiu, Colesiu: Bull. soc. chim., 49, 1291, (1931); Chem. Abstr., 26, 1245, (1932)

66. Conant, Aston: J. Am. Chem. Soc., 50, 2783, (1928); Chem. Abstr., 22, 4528, (1928)

67. Crippa, Long: Gazz. chim. ital., 61, 388, (1931); Chem. Abstr., 26, 144, (1932)

68. Clooz: (a) Compt., rend., 46, 344
(b) Jahresber. fortschr. Chem., 1853, 468
(c) Jahresber. fortschr.Chem., 1858, 344
(d) J. prakt. chem., (I), 74, 84

69. Curtius, Kastner: J. prakt. chem., 83, 215; J. prakt. chem., 44, 161; Chem. Abstr., 5, 2649, (1911)

70. Dakin, West: J. Biol. Chem. 74, 745, (1928); Chem. Abstr., 22, 2881, (1928)

71. Dalmer, Drehl, Walter: Ger. Pat. 663, 543 (Aug. 10, 1938), assigned to Firma E. Merck; Chem. Abstr., 32, 9099, (1938)

72. Dalmer, Walter: U. S. Patent 2,149,279 (March 7, 1939) assigned to Merck & Co.; Chem. Abstr., 33, 4271, (1939)

73. Dalmer, Walter: Ger. Pat. 632,257 (July 4, 1936) assigned to Firma E. Merck; Chem. Abstr., 30, 6894, (1936)

74. Dalmer, Walter: Canadian Patent 378, 818 (Jan. 10, 1939) assigned to Merck & Co., Inc.; Chem. Abstr., 33, 2147, (1939)

75. Dalmer, Drehl, Walter: U. S. Patent 2,176,063 (Oct. 17, 1940) assigned to Merck & Co., Inc.; Chem. Abstr., 35, 2157, (1941)

76. Daniels, Iwamoto: J. Am. Chem. Soc., 63, 257, (1941); Chem. Abstr., 35, 1390, (1941)

77. Davidson, Weiss, Jelling: J. Org. Chem., 2, 319, (1937); Chem. Abstr., 32, 1702, (1938)

78. Dorr, Mohring: Ger. Pat. 588,044 (Nov. 11, 1933) assigned to I. G. Farbenindustrie; Chem. Abstr., 28, 1354, (1934)

79. Dutta, Chandra De: Ber., 64B, 2606, (1931); Chem Abstr., 26, 1281, (1932)

80. Ellingson; J. Am. Chem. Soc., 63, 2524, (1941); Chem. Abstr., 35, 7408, (1941)

81. Ellingson, Henry, McDonald: J. Am. Chem. Soc., 67, 1711, (1945)

81a. Ellis: "Hydrogenation of Organic Substances", D. Van Nostrand Co., 3rd edit. (1930)

82. Endicott, Kornberg, Daft: U. S. Pub. Health Repts., 59, 49, (1944); Chem. Abstr., 38, 1564, (1944)

83. I. G. Farbenind. A.G. (Hans Schmidt, inventor): British Patent 485, 273 (Feb. 25, 1927); Chem. Abstr., 24, 919, (1930)

84. Fabriques de produits de chimie organique de Laire: French Patent 804, 391 (Oct. 22, 1936); Chem. Abstr., 31, 3507, (1937)

85. I. G. Farbenindustrie: Ger. Pat. 588, 044 (Nov. 11, 1933) Dorr, Mohring-inventor; Chem. Abstr. 28, 1354, (1934)

86, I. G. Farbenindustrie, A. G. : British Patent 476, 899 (Dec. 17, 1937); Chem. Abstr., 32, 3980, (1938)

87. Fenton: J. Chem. Soc. Trans., 1905, i, 804, (1905)

88. Fischer, Schoeller: Ann., 357, 1,; Chem. Abstr., 2, 813, (1908)

89. Fischer, Goldschmidt, Nussler: Ann., 486, 1, (1931); Chem. Abstr., 25, 1256, 3009, (1931)

90. Gabriel, Sonn: Ber., 40, 4850, (1907); J. Chem. Soc. Abstr., 1908, i, 60, (1908)

91. Gabriel, Stelzner: Ber., 29, 2384, (1896)

92. Gabriel, Sonn: Ber., 40, 4850, (1907); Chem. Abstr., 2, 851, (1908)

93. Gabriel, Lieck: Ber., 41, 1127, (1908); J. Chem. Soc. Abstr., 1908, i, 464, (1908)

94. Gabriel; Ber., 41, 1127, (1908); Chem. Abstr., 2, 2240 (1908)

95. Gabriel: Ber., 44, 57, (1911); Chem. Abstr., 5, 1426, (1911)

96. Gabriel: Ber., 46, 3859, (1913); Chem. Abstr., 8, 706, (1914)

97. Garelli, Racciu: Atti. accad. sci. torina, Classe sci. fis., 69, 182, (1934); Chem. Abstr., 29, 6326, (1935)

98. Gastaldi: Gazz. chim. ital., 51, (I), 233, (1921); Chem. Abstr., 16, 101, (1922)

99. Gastaldi, Princivalle: Gazz. chim. ital., 58, 412, (1928); Chem. Abstr., 23, 602, (1929)

100. Gastaldi, Princivalle: Gazz. chim. ital., 59, 751, (1929); Chem. Abstr., 24, 1383, (1930)

101. Gastaldi, Princivalle: Ann. chim. application, 26, 450, (1936); Chem. Abstr., 31, 3051, (1937)

103. Godchot, Mousseron: Bull. soc. chim., 51, 774, (1932); Chem. Abstr., 26, 5302, (1932)

104. Goulding: Masters Thesis, Univ. of Florida, 1944

104a. Green: "Industrial Catalysis", Macmillan Co., (1928)

105. Grosberg: U. S. Patent 2, 219, 839 (Oct. 29, 1940); Chem. Abstr., 35, 1066, (1941)

106. Gryszkiewicz-Trochimowski: Roczmiki Chem., 8, 165, (1928); Bull. soc. chim., 35, 366, (1924); Chem. Abstr., 22, 4476, (1928)

107. Gutknecht: Ber., 12, 2290, (1879)

107a. Heishberg, Huntress: Ind. Eng. Chem., Anal. Ed. 5, 344, (1933)

108. Hieber, Sonnekald: Ann., 456, 86, (1927); Chem. Abstr., 21, 3901, (1927)

109. Hill, Adkins: J. Am. Chem. Soc., 60, 1033, (1938); Chem. Abstr., 32, 4982, (1938)

110. Hinkel, Richards, Thomas: J. Chem. Soc., 1937, 1432, (1937); Chem. Abstr., 31, (1937)

111. Hofmann: Ber., 5, 247, (1872)

112. Hofmann: Ber., 23, 3724, (1890); J. Chem. Soc. Abstr., 60, 415, (1891)

113. Hofmann: (a) Jahresber. fortschr. chem., 1858, 343
(b) Jahresber. fortschr. chem., 1859, 358
(c) Compt. rend., 46, 256
(d) Compt. rend., 49, 782

114. Hofmann: (a) Ber., 23, 3297, (1890); J. Chem. Soc. Abstr., 60, 169, (1891)
(b) Ber., 23, 3711, (1890); J. Chem. Soc. Abstr., 60, 414, (1891)

115. Hortsman: J. Chem. Soc. Trans., 1905, 1, 804, (1905)

116. Ingram: J. Chem. Soc., 130, 692, (1927)

116a. Ipatieff: "Catalytic Reactions at High Pressures and Temperatures", Macmillan Co., (1937)

117. Japp, Knox: J. Chem. Soc., 87, 701, (1905); Ber., 32, 2206, (1899); J. Am. Chem. Soc., 7, 189

118. Joiner, Spoerri: J. Am. Chem. Soc., 63, 1929, (1941); Chem. Abstr., 35, 5896, (1941)

119. Jorre, Gabriel, Sonn: Dissertation at Kiel 1897; Ber., 40, 4855, (1907)

120. Karrer, Granacher, Schlosser: Helv. Chim. Acta., 6, 1108, (1923); Chem. Abstr., 18, 691, (1924)

121. Kauer, Kahnt, Isii, van Bergen: Helv. Chim. Acta., 21, 1174, (1938); Chem. Abstr., 33, 606, (1939)

122. Kaurer, Grancher: Helv. Chim. Acta., 7, 1062, (1924); Chem. Abstr., 19, 831, (1925)

123. Kindler, Peschke, Dehn: Ann., 485, 113, (1931); Chem. Abstr., 25, 1810, (1931)

124. Kitchen: Dissertation, Univ. of Florida, 1943

125. Kipping: J. Chem. Soc., 1932, 1336, (1932); Chem. Abstr., 26, 4053, (1932)

126. Knorr, Brownsden: Ber., 35, 4470, (1902)

127. Koop, Ditt, Hecksteden, Maier, Merz, Harle: Z. physiol. chem., 239, 30, (1936); Chem. Abstr., 30, 2583, (1936)

127a. Kuhn, Cook: Ber., 70, 761, (1937)

128. Kyrides: U. S. Patent 2,267,686 (Dec. 23, 1941); Chem. Abstr., 36, 2570, (1942)

129. Ladenburg: Ber., 23, 3740, (1890);

130. Ladenburg, Abel: Ber., 21, 758, (1888)

131. Lang: Ber., 42, 574, (1909); J. Chem. Soc. Abstr., 1909, i, 261, (1909); Chem. Abstr., 3, 1152, (1909)

132. Lang: Dutch Patent 229, 127; J. Chem. Soc. Abstr., 1911, i, 505, (1911)

133. Lang: Ger. Pat. 229, 127 (June 3, 1909); Chem. Abstr., 5, 2307, (1911)

134. Leslie, Watt: J. Org. Chem., 7, 73, (1942); Chem. Abstr., 36, 1902, (1942)

135. Levene, Steiger: J. Biol. Chem., 79, 95, (1928); Chem. Abstr., 22, 4472, (1928)

136. Levene, Schormuller: J. Biol. Chem., 106, 595, (1934); Chem. Abstr., 29, 122, (1935)

137. Ley, Schwarte, Munnich: Ber., 57B, 349, (1924); Chem. Abstr., 18, 2168, (1924)

138. Linstead, Noble: J. Chem. Soc., 1937, 911, (1937)

138a. Marek, Hahn: "The Catalytic Oxidation of Organic Cmpdt. in the Vapor Phase"; Am. Chem. Soc., series, No. 61, (1932)

139. Mason: J. Chem. Soc. Trans., 55, 97, (1889); J. Chem. Soc. Trans., 1893, 1284

140. Mason: Ber., 20, 267, (1887); J. Chem. Soc. Trans., 1889, 97, (1889)

141. Mason: J. Chem. Soc. Trans., 1893, 1284, (1893)

142. Mason, Dryfoos: J. Chem. Soc. Trans., 1893, 1293, (1893)

143. Mason Winder: J. Chem. Soc. Trans., 1893, 1355, (1893)

144. Mailhe, de Godon: (a) Compt. rend., 166, 467, (1918); Chem. Abstr., 12, 1383, (1918)
(b) Compt. rend., 166, 564, (1918); Chem. Abstr., 12, 1550, (1918)
(c) Compt. rend., 171, 1154, (1920); Chem. Abstr., 15, 1496, (1921)
(d) Compt. rend., 172, 1417, (1921); Chem. Abstr., 15, 3988, (1921)

145. Majert: U. S. Patent 471,420 (Mar. 22, 1892); Ger. Pat. 60,545 (Sept. 14, 1890); English Patent 15,404 (Sept. 29, 1890)

146. Majert: U. S. Patent 509,087 (Nov. 21, 1893)

147. Marckwald: U. S. Patent 500,665 (July 4, 1893)

148. McCombie, Parry: J. Chem. Soc., 95, 584, (1909)

149. Merck: British Patent 541,304 (Aug. 4, 1936); Ger. Pat. 632,257 (assigned to E. Merck & Co.); Chem. Abstr., 31, 219, (1937)

150. Michaelis: Ann., 373, 129, (1910); J. Chem. Soc., Abstr., 1910, I, 513, (1910)

151. McIlwain: J. Chem. Soc., 1943, 322, (1943); Chem. Abstr., 37, 6255, (1943)

152. Minovivi, Bente: Bull. sect. scil. acad. romaina., 4, 185, (1915); Chem. Abstr., 10, 606, (1916)

153. Moller, Birkofer: Ber., 75B, 1118, (1942); Chem. Abstr., 37, 5105, (1943)

154. Morera: Quin. e ind. 71, 303, (1929); Chem. Abstr., 24, 1644, (1930)

155. Morley: Ber., 12, 1793, (1878); J. Chem. Soc. Abstr., 88, 112, (1880)

156. Mullikin: "Compounds of Carbon", Vol. 2, page 89, Identification of Pure Organic Compounds

157. Narckwald: U. S. Patent 500, 665 (July 4, 1893)

158. Natenson: Ann., 98, 291, (1836)

159. Nueberg, Kansky: Biochem. Zeitsch., 20, 450, (1909); J. Chem. Soc. Abstr., 1909, i, 702, (1909); Chem. Abstr., 4, 1483, (1910)

160. Neresheimer, Roble: Ger. Pat. 670, 355 (Jan. 17, 1939); British Patent 476, 899 (Dec. 17, 1937) assigned to I. G. Farbenindustrie-A. G.,; Chem. Abstr., 33, 3173, (1939)

161. Novelli: Anales. asoc. quim. Argentia, 27, 161, (1939); Chem. Abstr., 34, 1659, (1940)

162. Ochiai, Tsuda, Ikuma: Ber., 68B, 1551, (1935); Chem. Abstr., 29, 7330, (1935)

163. Ochiai, Miyomato: J. Pharm. Soc. Japan, 57, 583, (1937); Chem. Abstr., 31, 6228, (1937)

164. Ochiai, Kakuda, Nakayama, Masuda: J. Pharm. Soc. Japan, 59, 462, (1939); Chem. Abstr., 34, 101, (1940)

165. Ornstein: U. S. Patent 2,008,923 (July 23, 1935); Chem. Abstr., 29, 5992, (1935)

166. Paden, Adkins: J. Am. Chem. Soc., 58, 2487, (1936); Chem. Abstr., 31, 683, (1937)

167. De Paoline: Gazz. chim. ital., 60, 700, (1930); Chem. Abstr., 25, 1493, (1931)

168. Petrow, Stack, Wiagg: J. Chem. Soc., 1943, 316, (1943); Chem. Abstr., 37, 6265, (1943)

169. Pfann: J. Am. Chem.Soc., 66, 155, (1944); Chem. Abstr., 38, 974, (1944)

170. Pollard, Adelson, Bain: J. Am. Chem. Soc., 56, 1759, (1934); Chem. Abstr., 28, 6130, (1934)

171. Pollard, Kitchen: Patent Application Serial No. 451, 048 (Filed July 15, 1942)

172. Poppenberg, Mayer: Ger. Pat. 657,979 (March 18, 1938); Chem. Abstr., 32, 5858, (1938)

173. Pratt, Young: J. Am. Chem. Soc., 40, 1428, (1916); Chem. Abstr., 12, 2323, (1918)

174. Princivalle: Gazz. chim. ital., 60, 298, (1930); Chem. Abstr., 24, 3792, (1930)

175. Raiziss, Clemence Freifelde: J. Am. Chem. Soc., 63, 2739, (1941); Chem. Abstr., 36, 427, (1942)

176. Riesz: French Patent 749, 152 (July 20, 1933); Chem. Abstr., 27, 5667, (1933)

177. Rimbock: U. S. Patent, 2,128,851 (Aug. 30, 1938); Chem. Abstr., 32, 8702, (1938)

178. Robinson, Siegel, Graessle: J. Pharmacol., 79, 354, (1943); Chem. Abstr., 38, 1028, (1944)

179. Rollins, Calderwood: J. Am. Chem. Soc., 60, 2751, (1938); Chem. Abstr., 33, 624, (1939)

180. Rudenburg: Ber., 46, 3555, (1913); Chem. Abstr., 8, 686, (1914)

181. Ruegsegger, Hamburger, Turk, Spies, Blankenhorn: Am. J. Med. Sci., 202, 432, (1941); Chem. Abstr., 36, 5896, (1942)

182. Sanna, Oliverio: Rend. seminar. facolta. scil. univ. Cafliari, 7, 104, (1938); Chem. Zentr. 1938, ii, 3086; Chem. Abstr., 34, 6285, (1940)

183. Sanna; Chem. Zentr., 1941, i, 1421; Chem. Abstr., 37, 1718, (1943)

184. Sanna: Chem. Zentr., 1933, i, 3315; Chem. Abstr., 28, 5823, (1934)

185. Sanna: Rend. seminar. facolta. sci. univ. Caglairi, 10, 40, (1940); Chem. Zentr., 1941, i, 1420; Chem. Abstr., 37, 1718, (1943)

186. Sausville, Spoerri: J. Am. Chem. Soc., 63, 3153, (1941); Chem. Abstr., 36, 425, (1942)

187. Schmidt, Sesler; J. Pharmacol., 77, 277, (1943); Chem. Abstr., 37, 2813, (1943)

188. Scholl, Eberle, Tritsch: Monatsh., 32, 1043, (1911); J. Chem. Soc. Abstr., 1912, i, 143, (1912)

189. Scholl, Eberle, Tritsch: Monatsh., 32, 1043, (1911); Chem. Abstr., 6, 867, (1912)

190. Schomaker, Pauling: J. Am. Chem. Soc., 61, 1769, (1939); Chem. Abstr., 33, 8065, (1939)

191. Schubart: U. S. Patent, 2,091,571 (Aug 31, 1937); Chem. Abstr., 31, 7446, (1937)

192. Scudi, Jelinek: J. Pharmacol., 81, 218, (1944); Chem. Abstr., 38, 5295, (1944)

193. Schwoegler, Adkins: J. Am. Chem. Soc., 61, 3499, (1939); Chem. Abstr., 34, 979, (1940)

194. Sesler, Schmidt: J. Pharmacol., 79, 117, (1943); Chem. Abstr., 38, 161, (1944)

195. Shuikin, Balandin, Duimov: J. Gen. Chem. (U.S.S.R.), 4, 1451, (1934); Chem. Abstr., 29, 3585, (1935)

196. Shuikin, Blandin, Plotkin: J. Gen. Chem. (U.S.S.R.), 4, 1444, (1934); Chem. Abstr., 29, 3584, (1935)

197. Shuikin, Bitakara, Brmilina: J. Gen. Chem. (U.S.S.R.), 6, 774, (1936); Chem. Abstr., 30, 6364, (1936)

198. Sieber: Ber., 23, 326, (1890)

199. Soc. des Usines chim. Rhone-Poulena: French Patent 698,687, (Oct. 7, 1929); Chem. Abstr., 25, 3013, (1931)

200. Sonn: Ber., 40, 4666, (1907); Chem. Abstr., 2, 823, (1908)

201. Spoerri, Erickson: J. Am. Chem. Soc., 60, 400, (1938); Chem. Abstr., 32, 2535, (1938)

202. Spoerri, Hall: J. Am. Chem. Soc., 62, 664, (1940); Chem. Abstr., 34, 2850, (1940)

203. Springer: Ger. Pat. 74, 628 (to Bayer & Co.) Friendlander's Fortschritte der Theerfarben fabrik. III, 957

204. Steiger, Treadwell: Ber., 15, 1059, (1882)

205. Stoehr: J. prakt. chem., (2) 47, 439; J. Chem. Soc. Abstr., 1893, 1, 486, (1893)

206. Stoehr: J. prakt. chem., (2) 48, 18,; J. Chem. Soc. Abstr., 1893, 1, 612, (1893)

207. Stoehr: J. prakt. chem., (2) 48, 191; J. Chem. Soc. Abstr., 1893, 1, 675, (1893)

208. Stoehr: J. prakt. chem., (2) 49, 392; J. Chem. Soc. Abstr., 1894, 1, 384, (1894)

209. Stoehr: J. prakt. chem., (2) 51, 449, (1895); J. Chem. Soc. Abstr., 1895, 1, 569, (1895)

210. Storch: Ber., 19, 2456, (1886); J. Chem. Soc. Abstr., 1886, 1044, (1886)

211. Stoehr, Detert: J. prakt. chem., (2) 55, 248, (1897); J. Chem. Soc. Abstr., 1897, 1, 442, (1897)

212. Takaki, Ueda: J. Pharm. Soc. Japan, 58, 44, (1938); Chem. Abstr., 32, 4149, (1938)

213. Takaki, Tsuda: J. Pharm. Soc. Japan, 58, 281, (1938); Chem. Abstr., 32, 5392, (1938)

214. Tamura: J. Bact., 47, 529, (1944); Chem. Abstr., 38, 5251, (1944)

215. Tanret: J. Chem. Soc. Abstr., 1885, 1, 1047, (1885)

216. Tiffeneau, Ditz, Levy: Bull. soc. chim., (5) 2, 1884, (1935); Chem. Abstr., 30, 1780, (1936)

217. Tota, Elderfield: J. Org. Chem., 7, 313, (1942); Chem. Abstr., 36, 6162, (1942)

218. Treadwell: Ber., 14, 1461, (1881)

219. Trevett: Bull. Johns Hopkins Hosp., 74, 299, (1944); Chem. Abstr., 38, 5593, (1944)

220. Tutin, Caton: J. Chem. Soc., 97, 2524, (1911); Chem. Abstr., 5, 1598, (1911)

221. Tutin: J. Chem. Soc., 97, 2495, (1911); Chem. Abstr., 5, 2853, (1911)

222. Vinaver: Khim. Farm. Prom., 1934, No. 6, 11,; Chem. Abstr., 30, 1796, (1936)

223. van Alphen: Rec. trav. chim., 54, 443, (1935); Chem. Abstr., 29, 5098, (1935)

224. van Alphen: Rec. trav. chim., 54, 937, (1935); Chem. Abstr., 30, 2196, (1936)

225. van Alphen: Rec. trav. chim., 61, 895, (1942); Chem. Zentr., 1943, ii, 1800; Chem. Abstr., 38, 5824, (1944)

226. Volkmann: U. S. Patent 482, 108 (Sept. 6, 1892)

227. van Arkel: Rec. trav. chim., 52, 1013, (1933); Chem. Abstr., 28, 2961, (1934)

228. Wallach: Nach. Ges. Wiss. Gottingen math. physik. Klass, 1927, 238; Chem. Abstr., 22, 2168, (1928)

229. Weijlard, Tishler, Erickson: J. Am. Chem. Soc., 67, 802, (1945); Chem. Abstr., 39, 3001, (1945)

230. Whitmore: Organic Chemistry 5th ed., pages 901-10

230a. Whitmore: J. Am. Chem. Soc., 54, 3274, (1932)

231. Wilson: Ger. Pat. 678, 154 (July 11, 1939) assigned Carbide and Carbon Chemical Co.

232. Wilson: U. S. Patent, 2, 136, 094 (Nov. 8, 1938); Chem. Abstr., 33, 1348, (1939)

233. Wilson: British Patent 497, 679 (Dec. 23, 1938); Chem. Abstr., 33, 3818, (1939)

233a. Winans, Atkins: J. Am. Chem. Soc., 54, 306, (1932); Chem. Abstr., 26, 969, (1932)

234. Wolff: Ber., 20, 425, (1887)

235. Wolff: Ber., 20, 721, (1887)

236. Wolff: Ber., 26, 724, (1893); J. Chem. Soc. Abstr., 64, 373, (1893)

237. Wolff: Ber., 26, 721, (1893); J. Chem. Soc. Abstr., 64, i, 373, (1893)

238. Wolff: Ber., 26, 1830, (1893); J. Chem. Soc. Abstr., 64, i, 612, (1893)

239. Wolff: Ber., 27, 2018, (1894); J. Chem. Soc. Abstr., 65, i, 548, (1894)

240. Wolff, Marburg: Annalen, 363, 169, (1908); J. Chem. Soc. Abstr., 80, 1, 16, (1909)

241. Wrede, Bruch, Keil: Z. Physiol. chem., 200, 133, (1931); Chem. Abstr., 26, 463, (1932)

242. Wood, Cork: "Pyrometery", page 41, 2nd ed., McGraw-Hill Book Co. (1941)

ACKNOWLEDGMENT

The author expresses his sincere appreciation to Dr. C. B. Pollard, Chairman of the author's Supervisory Committee, for his untiring guidance and counsel. Dr. Pollard's interest and directive suggestions have contributed immeasurably to the scope and success of this investigation.

The author extends his thanks to Associate Professor B. J. Otte, Curator of the Department of Chemistry, for his unfailing cooperation. The author is indebted to Mr. P. J. Thompson and to Mr. F. H. Hayes for the construction of special apparatus which expedited the completion of the research project. The author also extends his sincere appreciation to Mr. R. A. Carrigan for his spectrographic analyses of the catalysts used in this research project.

BIOGRAPHICAL ITEMS

C. E. Goulding, Jr. was born November 23, 1916 at Tampa, Florida. He pursued his undergraduate studies at the University of Tampa, where he received the Bachelor of Science Degree.

He has held the position of laboratory assistant for the past two years and at the present time holds a Graduate Council Fellowship. He is a member of the American Chemical Society.

COMMITTEE REPORT

This dissertation was prepared under the direction of the Chairman of the candidate's Supervisory Committee and has been approved by all members of the Committee. It was submitted to the Graduate Council and was approved as partial fulfilment of the requirements for the degree of Doctor of Philosophy.

Date May 27, 1946

T. M. Simpson
Dean

SUPERVISORY COMMITTEE:

R. B. Pollard
Chairman

H R Carroll

A. P. Black

J E Hawkins

Fred H. Heath.

COMMITTEE REPORT

This dissertation was prepared under the direction of the Chairman of the candidate's Supervisory Committee and has been approved by all members of the Committee. It was submitted to the Graduate Council and was approved as partial fulfilment of the requirements for the degree of Doctor of Philosophy.

Date May 27, 1946

T. M. Simpson
Dean

SUPERVISORY COMMITTEE:

C.B. Pollard.
Chairman

W. R. Carroll

A.P. Black

J. E. Hawkins

Fred H. Heath.